QUARTERLY REVIEW of PEDIATRICS

Vol. 4 No. 3 August 1949

"We have never had other iron salts so efficacious..."[1]

In the treatment of hypochromic anemia the new molybdenum-iron complex, Mol-Iron, is being found to possess *marked advantages* over equivalent dosage of ferrous sulfate alone, or combined with liver-stomach extract or folic acid.

Independent controlled tests[1, 2, 3] in relatively resistant iron-deficiency anemia of pregnancy have demonstrated a more rapid hemoglobin regeneration as well as greatly improved gastric tolerance. Investigators have commented: "The increases in hemoglobin (with Mol-Iron) were... dramatic and... rapid;"[1] there was "more rapid... response than with ferrous sulfate...;"[2] "unusually effective and well tolerated in... hypochromic anemia;"[3] "... encouraging results obtained with molybdenized ferrous sulfate in the microcytic hypochromic group indicate a better prognosis in these conditions (pregnancy anemia) in the future."[4]

1. Dieckmann, W. J., and Priddle, H. D.: Am. J. Obstet. & Gynec. *57*:541 (March) 1949.
2. Chesley, R. F., and Annitto, J. E.: Bull. Margaret Hague Maternity Hosp. *1*:68 (Sept.) 1948.
3. Healy, J. C.: Journal-Lancet *66*:218-221 (July) 1946.
4. Talso, P. J.: J. Ins. Med. *4*:31-34 (Dec.-Jan.-Feb.) 1948-1949.

White's **Mol-iron** *Tablets Liquid*

MOLYBDENIZED FERROUS SULFATE

A highly palatable Liquid; ideal for infants and children. Presents a specially processed, co-precipitated, stable complex of molybdenum oxide 3 mg. (1/20 gr.) and ferrous sulfate 195 mg. (3 gr.) in each teaspoonful (4 cc.). Bottles of 12 fluid ounces; also Tablets,—bottles, of 100 and 1000.

WHITE LABORATORIES, INC., Pharmaceutical Manufacturers, Newark 7, N. J.

BACKGROUND

ne use of cow's milk, water and carbohydrate mixtures represents the one system of

infant feeding that consistently, for over three decades, has received universal pediatric

recognition. No carbohydrate employed in this system of infant feeding enjoys so rich and enduring a background of authoritative clinical experience as Dextri-Maltose.

Fundamental for

"A mixture of several carbohydrates possesses certain advantages over a single sugar, as larger amounts of such mixtures usually may be fed without the danger of producing diarrhea."[1]

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***Mixed* Carbohydrate Liquid**

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"It must be emphasized that the baby needs vitamin D additions as soon as possible."[2] "Older children require prophylactic doses of vitamin D until maturity, especially during periods of rapid growth."[3]

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MILK DIFFUSIBLE VITAMIN D

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Drisdol—pure crystalline vitamin D_2—in Propylene Glycol is admirably adapted for use in the infant's formula as well as in milk, fruit juice, cooked cereals, etc. The daily dose is small—2 drops in milk for infants, and from 4 to 5 drops in milk for children or adults.

HOW SUPPLIED—Drisdol in Propylene Glycol—10,000 units per Gm.—in bottles of 5 cc., 10 cc. and 50 cc., with a dropper delivering 250 U. S. P. vitamin D units per drop.

healthy Babies

1. Marriott, W. McK.: Infant Nutrition, St. Louis, C. V. Mosby Co., 1941, p. 63.
2. Ibid. p. 96.
3. Kugelmass, I. N.: Newer Nutrition in Pediatric Practice, Philadelphia, J. B. Lippincott Co., 1940, p. 653.

NEW DRISDOL®
WITH VITAMIN A in (Sesame) Oil
NOW Also MILK Dispersible

Contains 50,000 U. S. P. units of vitamin A (from fish liver oil) and 10,000 U. S. P. units of crystalline vitamin D_2 (calciferol) per gram; 1250 U. S. P. units of vitamin A and 250 U. S. P. units of vitamin D_2 per drop.
DOSE: Same as Drisdol in Propylene Glycol.
SUPPLIED in bottles of 10 cc. and 50 cc.

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"The value of sulfonamide mixtures in reducing crystalluria and renal complications is based on undisputed experimental evidence."[1]

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Children—and adults who balk at bulky half-gram tablets—take ESKADIAMER willingly because it tastes good and is easy to swallow. Because ESKADIAMER is so unusually palatable, it is particularly useful when a prolonged course of therapy (as in prophylaxis) is indicated.

1. Lehr, D.: Sulfonamide Mixtures, J.A.M.A. 139:398 (Feb. 5) 1949

Eskadiamer

the delicious fluid preparation of sulfamerazine and sulfadiazine

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Each 5 cc. (one teaspoonful) contains 0.25 Gm. (3.86 gr.) microcrystalline sulfamerazine and 0.25 Gm. (3.86 gr.) microcrystalline sulfadiazine—the dosage equivalent of the standard 0.5 Gm. (7.7 gr.) sulfonamide tablet.

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QUARTERLY REVIEW OF PEDIATRICS

Vol. 4 No. 3 August 1949

Published quarterly in January, April, July and October. The annual cumulative subject and author index is bound in the October issue.

Subscription rate: $11.00 per year; $28.00 for 3 years.

WASHINGTON INSTITUTE OF MEDICINE

Editorial and Administrative Departments:
1708 Mass. Ave., N. W.
Washington 6, D. C.

Advertising Department:
2000 Connecticut Ave., N. W.
Suite 710
Washington 8, D. C.

Entered as second-class matter at the Post Offices at Washington, D. C., and Baltimore, Md., under the Act of March 3, 1879.

FOREWORD

The prime function of the QUARTERLY REVIEW OF PEDIATRICS is to make a survey, with a critical eye, of the important new contributions in every branch of pediatrics. Original reports are abstracted by pediatricians familiar with the subjects under consideration. The Editors and Editorial Board check over all abstracts and add interpretive or critical comments whenever necessary. The "Bookshelf" department reports informatively on new books the pediatrician should know about. Thus, within the covers of a single journal, there is brought together a concise chronicle of pediatric progress, well organized, reliable and complete. By exploring the entire expanse of medical literature the QUARTERLY REVIEW OF PEDIATRICS keeps its readers abreast of the most recent progress in all of pediatrics. A subscription to THE QUARTERLY REVIEW OF PEDIATRICS represents a continuous seminar on advances in pediatrics.

For convenience of reference the abstracts are grouped as follows:

1. Allergy
2. Anomalies, Genetics
3. Blood, Hemopoietic System
4. Cardiovascular System
5. Chemotherapy, Drugs, Poisons, Physical Agents
6. Clinical Pathology
7. Endocrine System
8. Eye, Ear, Nose and Throat
9. Gastrointestinal System
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The Pediatric Bookshelf
New Books, Pamphlets
Announcements

Issues of the QUARTERLY REVIEW OF PEDIATRICS appear in February, May, August, and November. A cumulative index for each volume is included in the November number. Suggestions, correspondence and editorial communications should be addressed to Irving J. Wolman, M.D., *Editor*, The Children's Hospital, 1740 Bainbridge Street, Philadelphia 46, Pa. Subscriptions should be mailed to the Washington Institute of Medicine, 1708 Mass. Ave., N. W., Washington 6, D. C. Annual Subscription: $11.00. Three years: $28.00.

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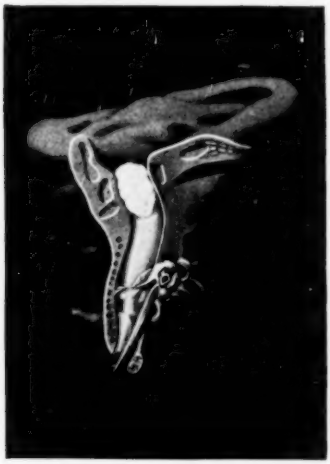
Middle Ear Disease



External Ear Disease

1. **Antibacterial**—local infection effectively attacked by high concentration of sulfa-urea.[1,2]
2. **Debriding**—infection site rapidly cleansed—odors reduced, and waste material removed.
3. **Analgesic**—pain and itching relieved by chlorobutanol.
4. **Fungicidal**—inhibits common fungous contaminants.
5. **Hygroscopic**—absorbs excess moisture, acts as decongestant.

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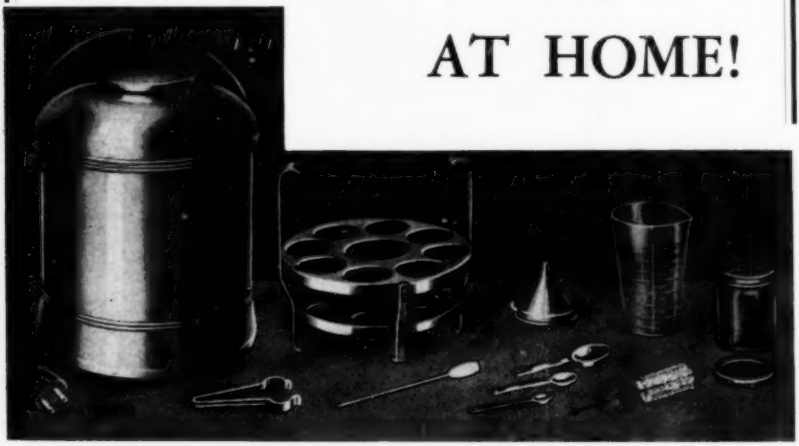
White's **OTOMIDE**

Topical Otologic Chemotherapy

WHITE LABORATORIES, INC. Pharmaceutical Manufacturers, Newark 7, N. J.

1. Holder, H. G., and MacKay, E. M.: Mil. Surg. *90*:509-518 (May) 1942.
2. Holder, H. G., and MacKay, E. M.: Surgery *13*:677-682 (May) 1943.

Hospital Technique
for Mother & Baby
AT HOME!



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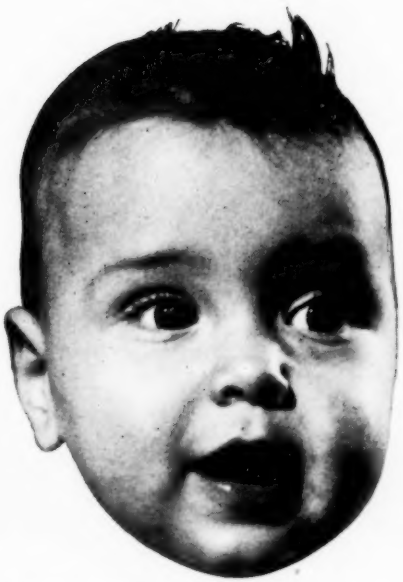

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Swift's Strained Meats easy to feed earlier

Soft, smooth Swift's Strained Meats are so fine in texture they may easily be bottle fed in the early weeks of life.

Some physicians start babies on these meats at two weeks—others as soon as the infant goes on solid foods.

Swift's Diced Meats—for older babies and young children—provide tender, bite-size pieces of meat that encourage chewing, aid teething. Swift's Diced Meats are tempting—help prevent anorexia in older babies. Six kinds: beef, lamb, pork, veal, liver and heart—help infants form sound eating habits.

Excellent source of complete proteins

Swift's Meats for Babies are an excellent source of complete, high-quality proteins . . . make available simultaneously all known essential amino acids—for optimum protein synthesis. In addition, Swift's Meats for Babies provide natural B vitamins and iron. As a food for growth and as a protective food meat has few peers. This is why so many doctors now recommend Swift's Meats for Babies for regular feeding early in life.

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in rheumatic fever and arthritis

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DECOSAL, containing Salicylamide, Succinic Acid and Ascorbic Acid, provides a unique salicylamide compound for prolonged and intensive therapy. Salicylamide is the drug of choice for unexcelled analgesic potency; succinic acid confers positive protection against salicylate toxicity. DECOSAL, a notable achievement in salicylate therapy, thus affords a new approach to the routine treatment of rheumatic fever and arthritis in providing prompt action and optimum absorption without unpleasant toxic or prothrombinopenic effects.

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A SIGNAL IMPROVEMENT

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Sodium salicylate ..... 5 gr.
Aluminum hydroxide gel, dried ..... 2 gr.
Calcium ascorbate ..... 1 gr. (equivalent to 50 mg. ascorbic acid)
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PLUS ANTACID
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"ASK YOUR DOCTOR"

CARNATION SINCERELY BELIEVES that the health of our nation's babies is too precious a thing to be left to the well-meant but doubtful advice of friends or relatives.

So year after year, month after month, Carnation advertising messages urge mothers to *go to their doctor* for advice on infant feeding. In an average month, Carnation newspaper, magazine and radio advertising repeats this advice 38 *million times*: "Ask your doctor."

And Carnation is proud to report that this consistent educational program is producing definite results. Here is the evidence:

8 OUT OF 10 MOTHERS USING CARNATION REPORT THAT IT WAS RECOMMENDED BY THEIR DOCTOR OR HOSPITAL.

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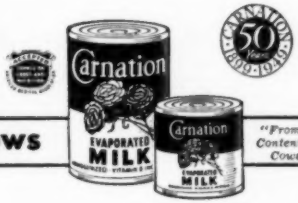

The Milk Every Doctor Knows

"From Contented Cows"


TURN Jeers
TO
CHEERS!
FOR MILK!
The extraordinary nutritional importance of milk in the dietary during infancy, childhood, pregnancy and old age — and for many gastro-intestinal and pre- and postoperative conditions — need not be lost to patients who are unable (because of personal dislike) to ingest it. Jeers for milk may be turned into cheers through the simple admixture of "Junket" Rennet Powder or Tablets. They transform milk into highly acceptable, deliciously flavored rennet desserts, which are eye-appealing and taste-tempting to young and old alike. These uncooked, custard-smooth rennet desserts in no way change the nutritional factors of milk, but they do facilitate easier, more rapid digestion because of the softer, finer, more flocculent curds produced in the stomach by the enzymic action of rennin.
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infant anorexia rapidly disappears

Just five drops daily of White's Multi-Beta Liquid stimulates the infant appetite; weight increase is favorably influenced and greater resistance to infection exhibited—the early infant's vitamin B intake is at a safe range.

Similarly in the adult, White's Multi-Beta Liquid, in teaspoon dosage, helps replenish and maintain adequate vitamin B stores—corrects deficiency-induced anorexia, aids in patient recovery, improves special or restricted dietaries.

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White's **MULTI-BETA LIQUID**

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Alhydrox*

Builds solid immunity step by step

Like Mr. McGinty's brick wall which stands solidly against the ravages of time because he builds it carefully, solidly, brick upon brick, the immunity you build with CUTTER "ALHYDROX" vaccine is solid.

"Alhydrox" *is a CUTTER exclusive*—developed and used exclusively by CUTTER for its vaccines and toxoids. It supplements the physician's skill by producing these immunizing advantages:

1. **"Alhydrox"** *adsorbed antigens are released slowly from tissue, giving the effect of small repeated doses.*

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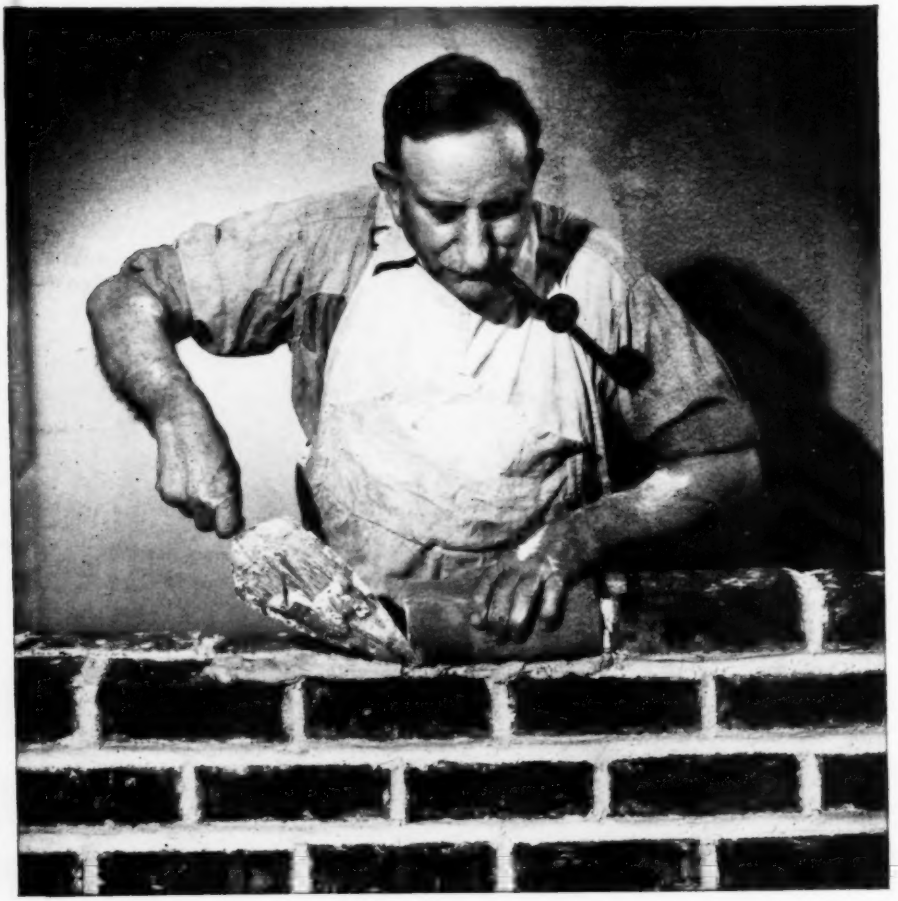

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The Pediatric Bookshelf

Announcements

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of their lives . . .

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HOFFMANN-LA ROCHE INC. • NUTLEY 10 • N. J.

Vi-Penta® Drops

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QUARTERLY REVIEW

of

PEDIATRICS

Volume 4 Number 3

August 1949

1. Allergy

Pollen Sensitivity in 100 Asthmatic Children. *Lewis Webb Hill, Harvard Medical School, Boston, Mass.* New England J. Med. 239:1039-40, Dec. 30, 1948.

Pollen sensitivity is common in asthmatic children and pollen sensitization and the common cold are the two most frequent causes of asthma in young patients. Of 100 consecutive cases of respiratory allergy studied in the office, 80 were cases of asthma and only 20 of hay fever, with a high proportion beginning as hay fever and progressing to pollen asthma. The author states that skin sensitivity to pollen in children is of lesser degree than in adults and that the intracutaneous test will often reveal sensitivity when the scratch test fails. A positive test in a child indicates clinical sensitivity. Scratch tests are done as a routine on all asthmatic patients, followed by intracutaneous testing of all pollen suspects with negative scratch tests. In 20 of the 30 children who failed to give a positive scratch test to any pollen, intracutaneous tests were positive to 1 or more pollens in 14 patients. In New England, birch and oak are the most important trees; maple pollen gives a great many positive reactions but is relatively unimportant as a cause of asthma because of its poor dissemination. Of the 100 patients, 68 showed grass pollen sensitivity, 28 by intracutaneous testing only. Seventy-three reacted to ragweed. No child reacted to pollen who did not also react to other environmental allergens, of which the most common were house dust, cat dander and one of the molds, especially alternaria or hormodendrum. The author doubts whether uncomplicated pollen allergy exists in asthmatic children. 1 table.

Management of the Pre-Allergic Child. *Bret Ratner, New York University College of Medicine, New York, N. Y.* Ann. Allergy, 6:629-38, Nov.-Dec., 1948.

Intra-uterine life, infancy, illness and convalescence constitute vulnerable periods during which every individual should be protected from undue exposure to highly antigenic substances. Every child is potentially allergic.

Much can be accomplished prophylactically by measures which aim to prevent food, dust, drug, serum and bacterial sensitivity through regulation of diet, management of environment, control of drug and serum therapy, and reduction of recurrent invasions by pathogenic agents. Man battles continuously against the invasion of foreign proteins. The difference between the normal individual, who battles successfully, and the allergic, who does not, is viewed by the author as dependent on quantitative rather than qualitative mechanisms both in respect to the amount of antigen to which the individual is exposed, and also the amount which actually penetrates the tissue cells.

The cardinal principles for a pregnant mother in order to avoid intra-uterine food sensitization of the unborn infant are: (1) a widely varied diet, (2) taking some of her food in "allergenically denatured" form, (3) no overeating, (4) no excessive indulgence in any single protein food or satisfaction of food cravings.

A newborn infant who receives one or several bottles of raw or dry cow's milk during the first two weeks and is then put back on the breast entirely, may develop milk sensitization which will not be evident until weaning is attempted. This form of sensitization may be prevented by prescribing an allergenically denatured milk for the relief formula, in conjunction with a denatured carbohydrate.

During severe gastrointestinal disturbances the permeability of the intestinal wall may be increased, to permit the ready entrance of unchanged protein into the blood stream. During treatment and convalescent care of severe intestinal disturbances, such as diarrhea, dysentery, and typhoid fever, one should give "allergenically denatured" foods, have a varied diet and avoid new foods and raw or lightly cooked foods. Similar considerations obtain during convalescence from other diseases. The practice of overfeeding infants and the present vogue for introducing many new foods very early in infancy also increase the tendency toward sensitization.

Early infancy and prolonged confinement to the sickroom are particularly vulnerable periods for development of sensitivity to specific dust allergens. In developing a prophylactic program every attention must be given to shield the bedroom from dustproducing elements, such as rugs, hangings, feathers and woollen materials. Infants and young children should not be permitted to sleep with pets or stuffed toys. To escape pollinosis, which results usually from undue exposure to pollens, the seashore or other sections of the country that are relatively free from pollen may be more advisable for vacation purposes. Insecticides which contain pyrethrum are potentially allergenic. Pyrethrum is closely related biologically to ragweed pollen.

Drugs in themselves are not antigenic, but may form antigenic conjugates in combination with proteins of the animal body. The phenolphthalein group of cathartics, the pyramidon and allonal drugs, external medicaments, have all resulted in specific sensitivity. The indiscriminate use of sulfonamide combinations and antibiotics should be curtailed. Caution should be observed in giving drugs to pregnant women and nursing mothers.

Knowledge concerning the pathogenesis of bacterial allergy is scant. It is difficult to diagnose and to differentiate it from the disease with which it may be associated. An allergic mechanism can lie behind the repeated common cold or coryza. It is likely that human beings are sensitive to one or more of the organisms in their respiratory tracts and that the degree of this sensitiveness fluctuates according to the recently existing local flora. All infectious processes in early infancy and childhood should therefore be meticulously treated, for the prevention of recurrent episodes should materially reduce the severity of the infections. Proper hygenic and dietary measures and judicious use of vaccines all help to prevent bacterial allergy. Pertussis, pneumonia, measles and scarlet fever often antedate asthma. Whether any direct relationship exists between these diseases and the subsequent allergy is difficult to determine.

Serum sensitivity can best be prevented by diminishing excessive contact with horses and rabbits, by desensitization of patients sensitive to animal dander, and by avoiding the indiscriminate use of antisera in meningitis, diphtheria or tetanus. 12 references.

(*The above recommendations are by one of the leading authorities in this field and merit serious attention, even though controlled studies of their effectiveness have not been reported. They seem particularly applicable to children with a strongly allergic family. Nevertheless not all students of the subject would agree that "every child is potentially allergic", and that "the difference between the normal and the allergic is dependent on quantitative rather than qualitative mechanisms."*

Although the allergist may not approve of it, "the present vogue for introducing many new foods very early in infancy" has many other advantages which will probably assure it of permanent acceptance. The foods need not be carried to extremes; because an infant is not made ill by getting meat at 6 weeks of age, he is not necessarily helped either. However, if the infant has learned to accept a variety of tastes and textures in food between 3 and 7 months, and has been allowed to develop a liking for them by avoidance of forced feeding, the feeding problems of later infancy which were once so common will seldom develop. Modern infants receiving varied diets seem much healthier than those of 20 years ago. For example, the severe epidemics of summer diarrhea persisted for many years after modern sanitary measures had been established and are still seen in mild form. The virtual disappearance of severe diarrhea has coincided with the introduction of modern infant dietaries, though the relationship has not been unequivocally proved.

Many pediatricians would be grateful for some definitive evidence of the value of bacterial vaccines. Many an allergic child's life is made even more miserable by his bi-weekly trips to the doctor's office for such injections.—ED.)

Growth Patterns of Allergic Children. *Milton B. Cohen and Lewis E. Abrams, Cleveland, Ohio.* J. Allergy 19:165-71, May 1948.

Wetzel Grids were used to demonstrate inherited tendencies toward slender physique, and to demonstrate growth failure caused by active allergy with subsequent growth repair when the allergy is controlled. Five hundred and three observations were utilized in constructing Grids for 150 allergic children; 622 observations were utilized in constructing Grids for 102 non-allergic controls.

Previous studies had indicated that the allergic child is likely to be short for his age and light for his height, presumably due to the effects of his disease. The present study shows, however, that these physical peculiarities are constitutional. By revealing deviations from the child's Grid pattern of direction and speed, the Grid technique indicates that active allergy disturbs the growth of affected children. 6 references. 4 figures. 2 tables.—*S. S. Stevenson.*

(*No one can quarrel with the authors' conclusion from their own data that active allergy disturbs the growth of affected children. Their first conclusion, however, that "allergy occurs more frequently in children (especially boys) who, by inheritance, are constitutionally slender" is not definitely proven or disproven by their data. In pointing this out this Editor is not implying that he disagrees with their concept — there is much suggestive evidence at hand to support such a hypothesis. He does disagree with the statement that channel position on the Wetzel Grid, or relative position on any other heightweight chart, can in itself prove the inherited nature of constitutional or bodily characteristics. The interplay between inherited or genetically determined characteristics and environmental factors starts with conception and is continuous for the remainder of the life cycle. If by the term "constitutional," as applied to a young child, we include the sum-total of all genetic and environment factors which are responsible for what that child is like at say, 4 or 5 years of age, then one might accept with equanimity the statement that allergy occurs more frequently in children who are constitutionally slender.*

For example: The child who habitually eats less of the requisite amount and type of food than he needs for proper nutrition will tend to be small for his age and light for his height, whether or not he be allergic. Anxiety states tend to predispose the child to allergic manifestations, and also to interfere with his appetite. The same environmental tensions which predispose a child to feeding difficulties also will favor the development of active manifestations of allergy. One must not attribute growth characteristics of selected groups of children to single agencies, unless the effect of all other potentially effective agencies have been measured and given proper weight.—ED.)

Intravenous Ethyl Alcohol in the Treatment of Status Asthmaticus in Children. *H. L. Bacal and S. Pedvis, Children's Memorial Hospital, Montreal, Que., Canada.* Canad. M. A. J. 59:410-12, November 1948.

The successful treatment of three children with status asthmaticus not responding to the usual drugs is presented with a discussion of the rationale of treatment. The material used is prepared by adding 50 cc. of 95 per cent ethyl alcohol to 1,000 cc. of 5 per cent glucose in saline. The action of this solution consists of: sedation, vasodilatation, bronchodilatation, respiratory stimulation, rapid metabolism and easily available calories. The cough reflex is stimulated and this helps to expectorate mucus. Fluid, electrolyte and sugar needs are also met. The advantages are: a nontoxic and nonallergenic solution without the undesirable side reactions of adrenalin, ephedrine, aminophyllin and the usual sedatives. It is effective in cases where these drugs have failed. After twenty-four hours, not only is the patient clinically improved but the chest is usually clear to auscultation. 80 to 100 cc. of the mixture is given intravenously in the first ten minutes, i.e., at a rate of 120 to 150 drops a minute. The remainder is given at the rate of 2 drops per kilogram per minute, the total being 40 cc. per kilogram of body weight. 11 references.—*Author's abstract.*

(*The hydration resulting from the intravenous injection of fluid is perhaps the important part of this treatment and is well known to all physicians. The addition of 50 cc. of 95% alcohol may be of some sedative value. However, not knowing whether the ill effects of the alcohol can be controlled, it would appear to be a safer procedure to use the glucose solution and administer phenobarbital or aspirin as a sedative. Perhaps one of the more important contributions to the treatment of status asthmaticus was that suggested by Ratner recently. He uses Syrup of Ipecac as an emetic which serves to treat the cause of the status, namely bronchial plugging. He also advocates intravenous fluid and steam inhalation as adjuvants.*—ED.)

2. Anomalies, Genetics

See Contents for Related Articles

3. Blood, Hemopoietic System

Recommended Terms and Definitions for Cells of the Erythrocytic Series.

Second Report of the Committee for Clarification of the Nomenclature of Cells and Diseases of the Blood and Blood-Forming Organs of the American Society of Clinical Pathologists and the American Medical Association. Am. J. Clin. Path, 19:57-60, January 1949.

It was the decision of the committee that none of the terms in current use for the nucleated cells of the erythrocytic series could be recommended

because mutually exclusive definitions for the same terms have been used in different schools of hematology, as well as for other reasons. After considering many suggestions the Latin stem *rubri* meaning red, was selected as least likely to be misinterpreted.

TABLE I.

Recommended Terms and Terms To Be Avoided When Referring To Specific Cells of The Erythrocytic Series.

NAME OF SERIES	TERM TO BE USED	TERM TO BE AVOIDED
Erythrocytic	Rubriblast	Erythroblast, megaloblast, pronormoblast, promegaloblast, normoblast, hemocytoblast, stem cell, myeloblast, lymphoidocyte, karyoblast.
	Prorubricyte	Erythroblast, megaloblast, pronormoblast, macronormoblast, macroblast, prokaryocyte.
	Rubricyte	Normoblast, pronormoblast, macronormoblast, erythroblast, polychromatophilic normoblast, karyocyte.
	Metarubricyte	Normoblast, erythroblast, metakaryocyte.
	Reticulocyte*	
	Erythrocyte	Red blood cell, erythroplastid, normocyte, akaryocyte.

* It is recommended that the reticulocyte stage be considered a subdivision of the erythrocyte stage.

The names selected for the stages of erythrocytic differentiation are given in Table 1. The qualifying adjective phrase *Pernicious anemia type* is applied to indicate the presence of the morphologic changes characteristically seen in pernicious anemia and other macrocytic anemias which respond to liver extract or folic acid therapy. Definitions are given for each of these cell types. 1 table.

Three Stage Analysis of Blood Coagulation. *J. H. Milstone, Yale University School of Medicine, New Haven, Conn.* J. Gen. Physiol., 31:301-324, March 20, 1948.

A method is presented for studying the activation of prothrombokinase, and further investigations of the entire clotting mechanisms are discussed.

A three stage procedure was used in which the experimental steps correspond with the three theoretical stages of the clotting reaction:

1. Activation of prothrombokinase
2. Activation of prothrombin
3. Coagulation of fibrinogen

The results first demonstrated that a definite latent period was present prior to the activation of prothrombin. This was shown to be the time necessary for the activation of a thrombokinase precursor. In conformity with prevalent usage, this activator complex was called prothrombokinase; it was realized, however, that it might contain more than one significant component. Calcium was found necessary for this reaction. The rate of activation of prothrombokinase was found to follow rather closely the curve for an autocatalytic reaction. In accord with this, it was also noted that thrombokinase apparently possessed the capacity to activate prothrombokinase.

The initial rate of prothrombin activity was found to depend upon the concentration of thrombokinase. Activation of prothrombin followed closely the theoretical lines of a unimolecular reaction. Calcium was also necessary for this stage. These findings were suggestive of an enzymatic reaction. It was also demonstrated, however, that thrombin does not catalyze the activation of prothrombin.

From the results obtained, all three reactions were considered enzymatic and the clotting mechanism was summarized as follows:

1. Prothrombokinase $\xrightarrow{\text{thrombokinase (?)/Ca}}$ thrombokinase
2. Prothrombin $\xrightarrow{\text{thrombokinase/Ca}}$ thrombin
3. Fibrinogen $\xrightarrow{\text{thrombin}}$ fibrin

8 figures. 3 tables. 33 references.—*J. H. Githens, Jr.*

Components of the Prothrombin Complex. *Armand J. Quick, Marquette University School of Medicine, Milwaukee, Wis.* Am. J. Physiol., 151:63-69, November 1947.

It has been clearly demonstrated by several workers that prothrombin has at least two components. The first is a labile factor which disappears in stored plasma, and was originally named component A by Quick. The other factor was considered the body of the prothrombin complex and is the principle which is diminished by the administration of dicumarol. This was termed component B by Quick.

Two families were studied in which several members of each had congenital hypoprothrombinemia Tests consisted of determining the prothrombin times on various combinations of the patients' plasma with other specimens of plasma in which either component A or component B had been removed. The results showed that the hypoprothrombinemia of the first family was due to a deficiency in component B. In the second

family, it was found due to a deficiency of a new and previously undescribed principle which is also essential of component A for prothrombin activity. Quick suggests the designation of component A for this principle instead of using that term for the labile factor.

Correlating this with previous work in various types of vitamin K deficiency, there is suggestive data that it is this new principle which decreases in vitamin K deficiency.

According to this concept, the equation for the formation of thrombin is:

Prothrombin (A and B) plus labile factor plus thromboplastin plus calcium = thrombin.

There is no evidence that any of these factors are enzymes.
4 tables. 16 references.—*J. H. Githens, Jr.*

The Value and the Limitations of the Coagulation Time in the Study of the Hemorrhagic Diseases.

Armand J. Quick, Rane Honorato and Mario Stafanini, Marquette University School of Medicine, Milwaukee, Wis. Blood, 3:1120-29, October 1948.

Trustworthy measurements of the intrinsic coagulative power of the blood can be obtained only by performing the test under constant and rigidly controlled conditions and by excluding all outside agents that influence the coagulation reaction. Since tissue juice contains thromboplastin, it is of utmost importance to exclude all traces from the specimen of blood used. Blood obtained by skin puncture (capillary blood) is unsuitable since it contains an appreciable amount of tissue fluid. Even in the taking of blood by venipuncture enough tissue thromboplastin may gain entrance to reduce the coagulation time significantly. The coagulation time may be prolonged in hemophilia, hypoprothrombinemia, afibrinogenemia and heparinemia. The author therefore recommends the following procedure for universal adoption. This procedure standardizes the three more important factors that influence the coagulation of blood in a test tube, namely, (1) temperature, (2) size of tube and (3) inner surface of tube.

Blood is drawn by venipuncture, preferably with a No. 22 needle, into a dry syringe. In drawing the blood the tourniquet should be applied just prior to the puncture. If blood is not obtained immediately and without trauma, another vein should be selected and a new puncture made. One cubic centimeter of blood is transferred into each of 2 scrupulously cleaned serologic test tubes (Pyrex 100 x 13 mm.) which have an internal diameter of 11 mm. The tubes are kept warm at 37 C. by being placed immediately in a water bath or a vacuum bottle containing water at this temperature and fitted with a hole in which the test tube can be inserted. The tube is gently tilted every 30 seconds and the end point taken as the moment when a flow of blood is no longer observed on tilting. The normal range is 5 to 10 minutes, with the majority of bloods clotting between 6 and 8 minutes. In normal blood, coagulation usually begins in 3½ to 4 minutes and is complete in 10 minutes, whereas in hemophilic blood the coagulation may

begin (to cite a specific observation) in 10 minutes but require 2 hours more before enough fibrin is formed for a solid clot. In hemophilia a coagulation time of one hour is not unusual, but two hours or more is rather infrequent, provided the test is done carefully and at 37 C. The coagulation time of a hemophilic individual may remain constant for a relatively long time.

In hemophilia little thrombin is formed since the plasma lacks the thromboplastin precursor, thromboplastinogen, which according to the authors' theory is activated by the enzyme present in normal platelets. Even after all the fibrinogen has coagulated, no demonstrable consumption of prothrombin has occurred. Thrombin, an enzyme, can convert all the fibrinogen to fibrin in a relatively short time. Only a few gamma of added thromboplastin are needed to coagulate 1 cc. of hemophilic blood. Even if the plasma contains enough thromboplastinogen to cause a normal coagulation time, it may not supply enough thrombin for the hemostatic needs. A normal coagulation time does not exclude a diagnosis of hemophilia.

In hypoprothrombinemia the coagulation time is so little increased that unless the test is done with great care the disturbance escapes detection. Only at very low levels do the prothrombin time and the coagulation time tend to become identical. The test is therefore of no value for a diagnosis of hypoprothrombinemia. In afibrinogenemia the blood is incoagulable. A small amount of fibrinogen restores the coagulation time to normal. Heparinemia, in man, has not been unequivocally demonstrated although there is a good probability that it can occur. The increase in coagulation time is not necessarily proportional to the concentration of heparin, but determination of coagulation time can be useful in controlling the therapeutic action of this drug. 19 references. 2 tables.

(*When laboratories are comparing data on coagulation time with one another it is obviously helpful if all the determinations have been done by a uniform method. Dr. Quick and co-workers here recommend a technic which standardizes the major variables in this test. This recommendation is greatly needed. We trust the technic will receive prompt and universal adoption.*

We have found that if the tubes of blood are held tightly in the human hand the contents remain essentially at body temperature for the interval required for normal blood to clot by the method here recommended. This minor change eliminates the need for a waterbath and simplifies the procedure appreciably. The test can be performed at the bedside or in the office with merely a scrupulously clean pair of test tubes (or even just one), needle and syringe. The house officer or practicing physician does not have to call on a clinical laboratory for assistance.

Some workers prefer to discard the first cubic centimeter of blood taken after venipuncture and substitute a fresh syringe to draw the specimen for testing.—ED.)

Idiopathic (Familial) Hypoprothrombinemia. *Paul S. Hagen and Cecil J. Watson, University of Minnesota Hospital, Minneapolis, Minn.* J. Lab & Clin. Med., 33:542-54, May 1948.

The authors summarize 13 reported instances of idiopathic hypoprothrombinemia as one basis for hemorrhagic diathesis, and describe a patient followed for a 10 year period. Several of the reported cases have been children. Familial hypoprothrombinemia has been demonstrated in at least four families.

The hemorrhagic disorder in this patient was characterized by epistaxis, subcutaneous hematomas, hemorrhages in various joints, and menorrhagia and metrorrhagia, the latter being so severe as to require hysterectomy. Symptoms began at the age of two years. The familial character of the disturbance was established by the finding that all members except the father showed prolongation of the prothrombin time. Only the mother and the patient noted easy bruising. The patient's 2-year old daughter was said to bruise easily but so far had had no episodes of bleeding.

Most of the blood and other laboratory studies were normal. The usual tests of hemostasis gave variable results. Sixty-three per cent of forty-nine clotting time determinations were prolonged. Forty per cent of 13 retraction studies were abnormal. Bleeding times were prolonged in 43 per cent of 46 tests. The cuff test was usually negative. The prothrombin times were consistently elevated. On comparing the recalcified clotting times of low and high speed centrifugalized plasma as outlined by Quick, the results were unlike those in hemophilia. The patient's plasma responded to added prothrombin in a manner similar to plasma made hypoprothrombinemic by oxidation or dicumarolization; the defect, therefore, did not seem to be an interference with prothrombin conversion. Other studies revealed no evidence of circulating anticoagulant, defect in fibrinogen, or delayed rate of convertibility. 21 references. 9 tables.

Hemophilia: Current Theories and Successful Medical Management in Traumatic and Surgical Crisis. *Claude-Starr Wright, Charles A. Doan, Verne A. Dodd, and James D. Thomas, Ohio State University, Columbia, Ohio.* J. Lab. & Clin. Med., 33:708-20, June 1948.

The primary impediment in the abnormal coagulation mechanism of hemophilia seems to be a retardation of the conversion time of prothrombin to thrombin. Calcium and a thromboplastic substance are necessary for this reaction, and in hemophilia there is a lack of available circulating thromboplastin. There is divergence of opinion with respect to the source or regulation of this catalytic or stoechiometric agent.

In the frozen state the antihemophilic activity of normal human plasma remains potent indefinitely and becomes readily available on rapid thawing in a water bath at 37 C. Restitution of frozen plasma requires rapid thawing in a waterbath at 37 C.; otherwise denaturation of the plasma proteins may occur with precipitation. Lyophilized plasma prepared within

a few hours after withdrawal from the donor has been reported to be as effective as the original plasma. The activity of all plasma diminishes rapidly after several days' storage even when kept at 4 C. Similar rapid diminution of the antihemophilic action has been observed in vivo. Benefit from transfusion of plasma or the concentrated antihemophilic fraction of Cohn lasts not more than seventy-two hours, irrespective of the amount given. On the basis of observations made repeatedly in severe hemophilic subjects, a maximal duration of effect can be obtained with 50 to 100 cc. of fresh plasma or restored frozen plasma. The concentrated unit of powdered plasma fraction I of Cohn when reliquefied with distilled water has a protein equivalent of 60 to 75 cc. of plasma, with an anti-hemophilic activity often to fifteen times the comparable volume of plasma from which it came.

The classic criteria for the diagnosis of true hemophilia include: (1) a familial history of the symptoms of hemophilia; (2) a personal history of more or less difficulty in controlling hemorrhage, especially following trauma; and (3) a prolonged coagulation time of venous blood. Shortening of the coagulation time after parenteral administration of one of the new anti-hemophilic globulin concentrates has proved a valuable confirmatory test. The differentiation of hemophilia from other hemorrhagic diatheses, as for example thrombocytopenic purpura or hypoprothrombinemia, is not always immediately possible during a clinical remission. When a specific abnormality or defect is not apparent on a single examination, repeated studies, particularly during symptoms, should be made.

The successful therapeutic management of hemophilia must include: (1) specific therapeutic agents to promote coagulation of the blood per se; (2) a prevention and guidance program to train the child with hemophilia early in life to adapt himself to the various limitations enforced by the disease; (3) intelligent utilization of physical therapy to overcome the otherwise frequently crippling hemarthroses.

Control of acute hemorrhage in the hemophilic person is approached from two angles: prompt parenteral treatment to maintain a normal coagulation time temporarily, and local application of hemostatic agents if possible. With appreciable blood loss, fresh whole blood will both provide the antihemophilic substance and replace the loss in red blood cells. Fifty cc. of freshly restored frozen or lyophilized plasma intravenously usually will maintain the coagulation time in a moderately severe hemophilic condition within safe limits for about twenty-four hours. One unit of Cohn's plasma fraction I (equivalent to 0.2 Gm. protein) will accomplish the same for from three to sixty-five hours. The intravenous and intramarrow routes have proved more reliable in reducing the coagulation time than the intramuscular route. If no veins are available the intratibial approach may be used.

A single venoclysis will generally control an acute hemorrhagic episode. In the surgical patient it is advisable to determine the coagulation time frequently, preferably three times daily. Two to three days' study of the

coagulation mechanism is desirable preliminary to elective surgery. Postoperative control should continue for from two to ten days, depending on the severity of the hemophilia and the extent of the surgery. It is also wise to employ local hemostatic agents at the operative site, such as fibrin foam or thrombin.

A refractoriness in the lowering of the coagulation time by fresh whole blood, plasma, or the plasma fraction I of Cohn after repeated administrations has been observed rarely.

The age range of forty-three hemophilic patients when first seen is given. Fifteen, or 34.8 per cent, were between 3 and 10 years of age. This age group presented the highest rate of hospitalization for hemorrhagic episodes, because normal physical activity and immaturity of perception make the child more subject to accidental trauma which initiates hemorrhage.

Many potential hazards can be overcome by an early guidance program. Collaboration of the physician, medical social worker, parents and school authorities can usually formulate a program of restricted activity which will allow the patient a relatively normal childhood while minimizing the acute hemorrhagic episodes and the tendency toward an invalid personality. 33 references. 1 tables. 5 figures.

Clinical, Hematologic, and Biochemical Studies on Twenty-five Cases of Hyperchromic Megaloblastic Anemia in Infancy. (*Rilievi anamnestico-clinici ematologici e biochimici e considerazioni patogenetiche su 25 casi di anemie iperchromiche megaloblastiche osservate in bambini della prima infanzia*). *Mauro Amato, University of Naples, Naples Italy.* Pediatria, 54:71-101, 1946.

Over a period of 4 years, 25 cases of megaloblastic hyperchromic anemia were observed in infants. The findings could not be reconciled to the picture of true pernicious anemia and a complete investigation was conducted to explain the pathogenesis.

The ages of the patients were from 3-21 months, the majority between 9-12 months. Evidence of the disease had existed for variable periods previously. An episode of acute febrile respiratory disease appeared to antedate the onset of anemia in most. Progressively increasing pallor was the presenting complaint in all.

All patients had various gastrointestinal disturbances which restricted them to human milk, but several had previously ingested a mixed diet. Suboptimal nutritional status and pallor were present and roentgenograms revealed no evidence of skeletal disease in any. Hepatomegaly and splenomegaly were always present. Hyperactive tendon reflexes were found in several, and one showed generalized hypertonia with fine tremors.

The red cell count varied from 0.72-1.95 million with a color index of 1.30-1.96 and increased cell diameter. Rare megaloblasts were seen in the peripheral blood and the reticulocyte count was normal. Neutropenia was common; platelet counts were low.

The bone marrow was examined in each and appeared hyperplastic with few normoblasts and a predominance of earlier red cell forms. Megakaryocytes were diminished in number. The granulocyte series was only slightly deviated to the left.

Red cell fragility was normal. Blood bilirubin was increased as was the serum iron. In 8 cases examined, there was no free gastric acid and a weak response total acidity after histamine. The urine revealed a slight increase of urobilin. The feces were negative for ova and parasites.

All patients responded promptly and without relapse to purified liver extract, some remaining completely well 4 years after therapy. Large doses of yeast extract alone in 4 failed to cause improvement. After an examination of the possible causes, a constitutional and functional inability to produce the intrinsic factor of Castle at birth is proposed. A variable congenital storage of the factor protects the infant during the first weeks. The mechanism for its normal production appears to be set into motion, permanently, by liver extract (antipernicious anemia factor). 66 references. 20 figures.—*A. M. Bongiovanni.*

(*The general description conforms to the type of anemia described by Cooley and Lee, J. Pediat.* 1:184, 1932, *which was believed to have a nutritional basis. For the most illuminating discussion of infantile megaloblastic anemia which has yet been published, with pertinent comments on this paper, see the abstract of Zuelzer's studies which follows this one.*—ED.)

The Syndrome of Megaloblastic Anemia in Infancy. *Wolf W. Zuelzer, Children's Hospital of Michigan, Detroit, Mich.* Vol. 1, Nutritional Anemia, Published by the Robert Gould Research Foundation, Cincinnati, Ohio, August 1948.

Megaloblastic anemia of infancy arises when the bone marrow organ becomes deficient in the hemopoietic principle contained in folic acid and in liver extracts. A syndrome of limited duration, it occurs in infants under 18 months of age, and is characterized by a normochromic and usually macrocytic anemia, megaloblastic dysplasia of the bone marrow cells, and anacidity or hypoacidity of the gastric juice. It responds specifically to therapeutic agents containing the hemopoietic principle. Permanent recovery follows a single adequate course of specific therapy; this feature distinguishes the syndrome from true pernicious anemia, which has a tendency to relapse and is exceedingly rare in infants.

A combination of factors, rather than a single element, seems responsible usually for the condition. A constitutional element is suggested by the racial distribution of the patients. Amato's 25 patients reported from Italy in 1946 (preceding abstract), 36 infants studied by the author, and all others reported thus far belonged to the white race. Few cases have been reported among Negroes. A certain physical type was predominant in the author's series. "With one or two exceptions these infants were of fair complexion with blonde hair, blue eyes, and a skin of delicate texture. A prominent,

square forehead was often noticed". The role played by heredity is obscure. The condition seems limited to infants between the ages of 3 and 18 months, with a peak incidence between 9 and 12 months.

Growth, diet, and infection all have contributory roles in causation. Hemopoiesis is most active in infancy, and a relative or absolute deficiency of any of the necessary substances can be expected to produce anemia more easily and more rapidly than at any other time. The case histories seldom indicate a duration of more than a few weeks. Further evidence for the importance of growth is seen in the early development of the condition in premature infants, whose growth rate is especially rapid. Of nine patients under four months of age at the onset of the anemia, six were prematurely born, though only seven of the total series of 36 patients, including a pair of twins, were born prematurely. All of Amato's patients were full term infants, and there was a little evidence to suggest that an inadequate maternal diet during gestation was a contributory factor in a few of the patients. There was no indication that the maternal nutrition was unsatisfactory in the author's group.

In analyzing the basic diet of the 36 infants the author found 21 who had been given milk mixtures of comparatively low protein content. Their feedings had been dilutions of proprietary products of dried cow's milk which attempt to simulate the composition of breast milk. All of the 25 patients reported by Amato had been breast fed and it is possible that the breast milk produced by mothers subsisting on a wartime diet in Southern Italy was deficient in quantity and probably also in specific accessory substances; many of these infants were past the age when breast milk alone is considered a complete diet, yet they were not receiving supplementary foods. In the author's series the body weight was below average in well over half the patients and low levels of serum protein were present in nearly every case. Many had recently had gastrointestinal disturbances. Only 11 of the 36 had received or eaten solid foods, though the majority were at an age when the milk diet is usually supplemented. Sixteen had failed to receive orange juice or Vitamin C preparations in adequate amounts, if at all, and eight were suffering from scurvy. The high incidence of scurvy illustrates the poor general state of nutrition of these infants, and makes it likely that other dietary deficiencies existed at the same time. Although rickets was not encountered, osteoporosis was noted in films of the skeleton in 8 cases, in addition to those with frank scurvy. Of four other patients, two had received only goat's milk, and two were exclusively breast fed. Evidently goat's milk is low in some factor which normal human or cow's milk supplies in adequate amounts.

Of the two breast fed infants in the group, one mother had pernicious anemia, and the other mother had hypochromic anemia with glossitis and achlorhydria. The development of megaloblastic anemia in these infants suggests the absence of a specific factor in the milk of women with certain types of anemia accompanied by achlorhydria.

There were, accordingly, 24 patients whose diet may have been suboptimal in one way or another. In one other the dietary history was not specified. The remaining 11 had received appropriate mixtures of whole cow's milk or of standard commercial brands of evaporated or homogenized milk, and several also had had adequate supplements of solid foods and vitamins.

Nearly every patient showed signs of active infection at the time of hospitalization and in most instances the illness had been ushered in by symptoms of infection. This relation to infection had also been noted by Amato. Respiratory infections predominated. The infections rarely seemed severe, and there was no correlation to the degree of anemia. Some had marked anorexia, or vomiting and diarrhea, but others ate well and were free from gastrointestinal disturbances. Absorption, nevertheless, may have been impaired as suggested by the finding of histamine-refractory achlorhydria in nearly every case, both in this series and that of Amato. It remains to be seen if the achlorhydria is a pathogenetic factor or merely a concomitant finding in megaloblastic anemia. In all but one case retesting after disappearance of the infection showed normal or nearly normal values for free gastric hydrochloric acid.

These considerations lead to the conclusion "that megaloblastic anemia is not a single disease of uniform causation but usually results from a combination of several factors: a constitutional racial background, a predisposition due to age, general and perhaps specific dietary deficiencies, and nonspecific infection, rarely from anatomic or functional interference with absorption of substances from the intestinal tract."

The signs and symptoms of megaloblastic anemia are those of anemia in general, though often overshadowed by manifestations of the associated infection or deficiency states. The physical findings are not characteristic. Pallor is marked. The liver is nearly always enlarged, with enlargement of the spleen at times. Fever is virtually constant.

The laboratory findings in advanced cases are essentially identical with pernicious anemia. There is anemia with macrocytosis, leukopenia and thrombopenia, also Howell-Jolly bodies, Cabot rings, punctate and diffuse basophilia, anisocytosis, poikilocytosis, nucleated red cells with megaloblastic features, and hypersegmented and giant neutrophile leukocytes. The white cell count is often moderately elevated, probably because of the presence of infection. A relative neutropenia is the rule. In the early stages macrocytosis may not be pronounced. The bone marrow findings are essentially those obtained in pernicious anemia in relapse, though without the absolute erythroid hyperplasia. In the incipient stages erythropoiesis is predominantly megaloblastic, but many of the erythroblasts have an appearance intermediate between normoblasts and classical megaloblasts. The plasma usually has an elevated bilirubin content. Hypoproteinemia is almost constant. Amato found the serum iron of his patients consistently elevated and the urobilinogen

excretion in feces and urine distinctly increased. "The temporary absence of free hydrochloric acid from the gastric juice, even after injection of histamine, is so nearly constant that it almost constitutes a diagnostic criterion."

The nature of the marrow disturbance seems comparable in every respect to that of pernicious anemia. There is disturbance in mitosis affecting chiefly the better-differentiated marrow elements which ordinarily are most active in reproduction. Mitotic activity becomes confined largely to primitive cells, few of which mature and reach the blood stream.

Treatment must be directed against the underlying infection or other associated conditions, as well as against the disturbance in hemopoiesis. Immediate blood transfusion is often indicated and may prove life saving. The anemia itself responds dramatically to purified or crude liver extract or to folic acid within 24 hours after the first parenteral dose of either substance. The bone marrow improves so rapidly that a morphologic diagnosis becomes almost impossible within 36 hours after start of therapy. Usually by 3 to 6 days a reticulocyte crisis is observed and the hemoglobin and red blood count begin to rise. The treatment employed at present consists of parenteral injections of 20 mg. of synthetic folic acid, daily, for one week. If liver extract is used, one or two injections of 15 USP units of purified extract are sufficient. Vitamin supplements are also given.

The prognosis is excellent. All patients who did not succumb to the associated disease made a permanent recovery. Some recovered permanently following transfusion alone. 10 references. 6 figures. 1 table.

(*This article is given an extended summary because it represents a definitive presentation of an important newly described disease, and the full report will undoubtedly not be seen by many of our readers.*—ED.)

Interpretation of Rh Antibodies. *I. Davidsohn and Kurt Stern, Mount Sinai Medical Research Foundation, Chicago, Ill.* Am. J. Clin. Path. 18:690-99, September 1948.

There are four different technics for Rh antibodies: 1. The test in which saline is used as diluent; 2. the test in which human serum or plasma or bovine albumin is used as diluent; 3. the test for blocking antibodies; 4. the Coombs test (Hill's developing test). Results are given of some of these tests in 182 pregnant women. Of these women, 40.1 per cent had blocking antibodies.

When the highest titer of serum albumin agglutinins was 1:10 or less, about one-third of the children died. When the highest titer was above 1:10, about two-thirds of the children died. The mortality was (in round numbers): 71 per cent with an agglutinating titer above 1:10 and with blocking antibodies, 43 per cent with an agglutinating titer less than 1:10 and blocking antibodies, 61 per cent with an agglutinating titer above 1:10 without blocking antibodies, but only 28 per cent with an agglutinating titer of 1:10 or less without blocking antibodies. Thus the outcome of

pregnancy and the chances of survival of the infant are made less favorable by the finding of blocking antibodies, except when such antibodies may have been carried over from a previous pregnancy or when the father is heterozygous. 5 references. 6 tables. 1 figure.

Reproductive Histories of the Mothers of 322 Infants with Erythroblastosis. *Edith L. Potter, The University of Chicago and the Chicago Lying-in Hospital, Chicago, Ill.* Pediatrics 2:369-81, October 1948.

An analysis was made of the reproductive histories and the phenomena of erythroblastosis of 175 women observed since 1934 who became immunized to the Rh factor at some time during their reproductive careers, a total of 699 pregnancies. Three hundred and forty-one pregnancies preceded the birth of the first infant with erythroblastosis. These resulted in seven stillbirths, 13 neonatal deaths, 65 abortions and 256 surviving children. Forty-four of these abortions occurred between the birth of the last normal child and the birth of the first child with erythroblastosis. Four of these women had had earlier transfusions.

Ninety-six women had 179 pregnancies following the birth of an earlier infant with erythroblastosis. These have ended in the birth of 3 Rh-negative infants, 144 Rh-positive infants with erythroblastosis, and 32 abortions (13 induced). Of these Rh-positive infants, 69 were stillborn, 63 died and only 12 survived. Three of the latter have brain damage.

The previous maternal history has been of more value in prognosticating the fate of an infant born to an immunized Rh-negative woman than have changes in maternal antibody titer or differences in the variety of antibodies present. 1 reference.

Exchange Transfusion in Hemolytic Disease of the Newborn. *P. L. Mollison and M. Cutbush, Postgraduate Medical School, London, England.* Lancet 2:522-37, Oct. 1948.

Thirty newborn infants with erythroblastosis fetalis were given exchange transfusion via the umbilical vein. These were all infants whose cord blood had either a hemoglobin below the normal range, or a bilirubin value above the normal range, or both. Twenty ml. amounts of blood were exchanged successively until about 350 to 450 ml. had been withdrawn and replaced by Rh-negative blood. The exchange transfusions were most often carried out within 13 hours of birth (23 cases). In the remaining 7 cases they were done 17 to 38 hours after birth. Only about 7 of the infants were given prophylactic chemotherapy but it is advised that all such infants be given prophylactic doses of penicillin for 48 hours afterwards.

No ill effects attributable to the procedure were seen. A transparent polyethylene catheter is preferred so that minute air-bubbles can easily be seen and their introduction into the infant's circulation avoided. The blood given was made slightly concentrated by removing some of the supernatant citrated plasma immediately before use.

Of the 30 infants treated by exchange transfusion, 7 died and 23 recovered. One infant who died had hydrops fetalis; 3 had severe anemia, were in critical condition at birth and died within 24 hours; 3 had developed profound jaundice despite exchange transfusion and died 2 to 4 days after birth. Only one of the 23 survivors shows signs of damage to the central nervous system. Among the survivors were several infants whose condition was very critical at birth.

Serologic measurements showed that the amount of free Rh-antibody removed by exchange transfusion was less than would be expected if the infant's total amount of antibody were present in the plasma at the beginning of the transfusion. Removal of antibody from the plasma seems to lead to the entry into the plasma from the tissues of a further amount so that a new equilibrium is reached at a slightly lower level.

Because of the difficulties in securing good control series, the value of exchange transfusion in lowering mortality and morbidity must still be considered unproved. It can justifiably be used as the most convenient method of treatment available. It is not a trivial procedure, and should be reserved for cases where a single transfusion of Rh-negative blood is not likely to suffice.

From review of the data of 63 infants with erythroblastosis fetalis (33 not treated with exchange transfusion) the authors advise that the severity of a case of hemolytic disease of the newborn can be assessed reliably from an examination of cord blood. They suggest that, if exchange transfusion is to be used as a method of treatment, it should be carried out only if the hemoglobin of the cord blood is below the normal range (say, below 14.5 Gm. per 100 ml.) or if the bilirubin value of the cord blood is above 4 mg. per 100 ml. (normal range 0.5 to 2.5 mg. per 100 ml.). When the hemoglobin is just below 15 Gm. per 100 ml., or the bilirubin concentration is 3 to 4 mg. per 100 ml. the finding in a blood film of an excess of nucleated red blood-cells (say, more than 10 per 100 white cells) should decide the issue in favor of an exchange transfusion. If cord blood has not been examined, the appearance of jaundice of the skin within 12 hours of birth in an infant whose blood gives a positive direct Coombs test is an indication for exchange transfusion. 16 references. 2 tables. 1 graph.

Studies on the Rh Hapten. *Bettina B. Carter, Western Pennsylvania Hospital, Pittsburgh, Pa.* Penna. M. J. 52:124-27. November 1948.

A hapten is a specifically reacting fraction of an antigen which will combine with antibody in vivo and in the test tube, but which will not evoke antibody when injected alone into the experimental animal. A method is described for isolation of the Rh hapten from Rh-positive red cells. The author proposes as the standard unit for measuring its activity the least quantity required to fix two full units of complement in the presence of an agglutinating anti-Rh (anti-D) serum of titer of 32.

Rh hapten is apparently a lipid substance. It will not produce antibodies when injected into guinea pigs except when coupled with an antigenic protein such as egg albumin. Finished Rh hapten preparations have remained constant in activity for at least three months and some lots have retained their strength for indefinite periods.

This hapten is being studied clinically in relation to both active and passive Rh sensitization. From 500 to 1500 units of Rh hapten have been given intramuscularly to sensitized Rh-negative mothers. The initial injection may be followed by others in from one to two weeks and at intervals throughout pregnancy. Consecutive titrations of serum drawn from 30 treated sensitized women have shown falls in titer in 30 to 32 cases treated to date. Treatment is begun preferably as soon as pregnancy is established or as soon as sensitization is revealed in Rh-negative women who are pregnant. There have been no untoward reactions, either systemic or local, from the administration of Rh hapten and there is no evidence that the hapten has any antigenicity in human beings.

Babies delivered from treated women have been normal so far in all but two cases. These two cases have involved mothers who had lost erythroblastotic babies previously and who were severely sensitized.

Erythroblastotic babies, i.e., those born of untreated, Rh-sensitized mothers, have been given from 1000 to 6000 units of Rh hapten intramuscularly. Of twenty-five babies treated with Rh hapten, nineteen recovered and developed normally. Six babies died, but in five of these cases the physicians felt that the cause of death was not erythroblastosis. This series includes only severe cases. 2 references.

(*This decade has witnessed immense strides in medical understanding of the nature of the disturbances responsible for erythroblastosis fetalis. A series of advances have occurred in rapid succession—the discovery of the Rh factor itself, the demonstration of anti-Rh antibodies and their relation to erythroblastosis fetalis and many hitherto obscure transfusion reactions, the recognition that there are not one but three Rh factors, the manifest value of repeated transfusions of Rh-negative blood in affected infants, and so forth. One of the major problems still remaining unsolved is that of prophylaxis, which is just about as baffling now as it ever was. The Rh hapten represents a new and ingenious concept in the search for an effective desensitizing agent. One hopes fervently that it will prove successful in more extensive and critically controlled series of cases.*—ED.)

Massive Necrosis of Liver Following Exchange Transfusion for Erythroblastosis Fetalis. *Philip Rosenblatt, The Jewish Hospital and the Kingston Avenue Hospital for Contagious Diseases, Brooklyn, N. Y.* Am. J. Clin. Path. 18:700-715, September 1948.

Fatal liver necrosis occurred in three infants with erythroblastosis fetalis and in one infant with calcium gluconate intoxication. In the cases of erythroblastosis, the diagnosis was made antenatally by means of serologic

tests, the pregnancies were terminated by caesarean section before term, and the babies were transfused immediately by the exchange or substitution technic. Death occurred at one to five days; at necropsy all showed massive liver necrosis, and two also had focal necroses in the adrenal glands. These changes were attributed to the blood transfusions rather than to the erythroblastosis alone. The author suggests that a combination of factors may have been responsible for these untoward findings: (1) the erythroblastosis; (2) the presence of excessive amounts of sodium citrate or calcium gluconate in the transfused blood; and (3) excessive speed of transfusion. The use of heparinized rather than citrated blood is therefore recommended since this would obviate the use of sodium citrate or calcium gluconate. It is advised that exchange transfusions be given slowly. 25 references. 8 figures.

(*Inasmuch as erythroblastosis itself can give rise to necrosis of the liver, one must await the gathering and analysis of large series of cases before one can be certain that the liver lesions in these 3 cases were due to the underlying disease or to the transfusion program.*—ED.)

Studies on Free Erythrocyte Protoporphyrin, Plasma Iron and Plasma Copper in Normal and Anemic Subjects. *G. E. Cartwright, C. M. Huguley, Jr., Helen Ashenbrucker, B. A. Jane Fay, and M. M. Wintrobe. School of Medicine, University of Utah, Salt Lake City, Utah.* Blood 3:501-25, May 1948.

This paper presents the results of studies on free erythrocyte protoporphyrin, plasma iron, and plasma copper in normal subjects and in subjects with various types of anemia. Of interest to pediatricians are some of the observations on anemic states. In the anemias due to iron deficiency and to infection the free erythrocyte porphyrin and copper were elevated, whereas the plasma iron was diminished. In nephritis with anemia the erythrocyte protoporphyrin was generally increased, the plasma iron low or normal and the plasma copper increased. Anemia associated with lymph node disorders or leukemia was accompanied by a normal or high erythrocyte protoporphyrin, a low or normal plasma iron and an increase in plasma copper. Thalassemia major was found to be accompanied by both hypercupremia and hyperferremia. In thalassemia minor the serum iron values were normal but hypercupremia was found. Hyperferremia was noted in aplastic anemia.

Interpretation of these findings is not always clear, but certain principles seem to stand out. In general it was found that in conditions characterized by hypoferremia, the erythrocyte protoporphyrin and plasma copper are elevated. There is an increase in erythrocyte protoporphyrin in anemic states associated with a normoblastic bone marrow due to a disturbance in hemoglobin synthesis, i.e., iron deficiency, anemia of infection, nephritis, lead poisoning and some cases of "lymphoma" and leukemia. In conditions in which the amount of iron absorbed is decreased (inadequate dietary intake of iron, etc.) and in conditions in which the rate of elimination is increased (hemorrhage), the plasma iron is low. In conditions in which the amount of iron

going to the tissues is increased (anemia of infection), the plasma iron is low. In conditions in which hemoglobin synthesis is reduced due to factors other than a lack of iron (pernicious anemia in relapse, thalassemia major, aplastic anemia) the plasma iron is high. In conditions in which hemoglobin catabolism is accelerated (hemolytic anemia) the plasma iron is high. So little is known of the function and metabolism of copper in relation to the red cell that interpretations of the findings with respect to copper are not possible. 30 references. 11 tables.

(*Iron forms but a small fragment of the hemoglobin molecule*—0.34 *per cent to be precise. There is great need for more information with respect to the non-iron moiety of hemoglobin and the status of the hemoglobin precursors of the blood plasma in normal subjects as well as in those with disease states. Out of such fundamental studies as here summarized may come very significant advances in the therapy of the anemias.*—ED.)

Osmometric Behavior of Normal and Abnormal Human Erythrocytes. *George M. Guest, Children's Hospital Research Foundation, and the University of Cincinnati, College of Medicine, Cincinnati, Ohio.* Blood 3:541-55, May 1948.

Two main principles seem to govern the swelling and hemolysis of red blood cells suspended in hypotonic salt solutions: the cells imbibe water according to the laws of osmosis, and their maximal swelling is limited by an inelastic surface membrane. According to this concept, hemolysis occurs when the red cells in hypotonic solutions attain a critical volume at which the cells rupture and allow escape of hemoglobin. Normal human red cells suspended in the hypotonic salt solutions employed for testing red cell fragility behave like nearly perfect osmometers, with their maximal swelling, usually around 175 per cent of the initial volume, sharply defined by their mean surface area.

The same principles govern the swelling and hemolysis of some abnormal types of red cells. In congenital hemolytic icterus the red cells exhibit essentially normal osmotic behavior, but since the spherocytes can swell very little within the limits of their surface area they rupture at higher tonicities, with the maximal swelling in most instances around 150 per cent of their initial volume. Thin cells are capable of greater swelling than normal cells.

Red cells of patients with Mediterranean anemia, sicklemia and pernicious anemia exhibited less than the expected osmometric swelling throughout the series of hypotonic solutions and displayed varying patterns of hemolysis and of maximal swelling. The increased osmotic resistance characteristic of the cells of Mediterranean anemia is accounted for by two mechanisms: they swell less than normal cells at each tonicity; and, being thin, they undergo greater swelling (around 220 per cent) before being hemolyzed.

The method employed was that of suspending red cells in graded series of hypotonic salt solutions in a special Van Allen pipette, centrifuging the

unhemolyzed cells after one hour, measuring the volume of these cells on the graded pipette stem, and determining the content of laked hemoglobin in the clear supernatant to obtain the extent of the hemolysis.

Interestingly, the cells in a few subjects with the latent or carrier states of Mediterranean anemia and sickle cell anemia followed more closely the normal expected pattern, (but with a maximal value of about 200 per cent) then did the cells of individuals in the active phases of these diseases. 25 references. 7 figures.

(*Altered osmotic fragility of the red cells is one of the cardinal findings in congenital hemolytic anemia, sickle cell anemia and Mediterranean anemia. One of the easiest ways of recognizing an asymptomatic "carrier" with any of these hereditary forms of anemia is to check on the osmotic resistance of his red cells. These experiments by Guest represent an effort to determine what lies behind the altered osmotic resistance.*—ED.)

Sulfhydryl Compounds and the Sickling Phenomenon. A Preliminary Report. *Lewis Thomas and Chandler A. Stetson, Jr., Johns Hopkins University Medical School and Johns Hopkins Hospital, Baltimore, Md.* Bull. Johns Hopkins Hosp. 83:176-80, August 1948.

Addition of solutions of hydrogen sulfide, BAL or cysteine to red blood cells from patients with sickle cell anemia produces rapid and complete sickling. Hydrogen sulfide is most effective, producing sickling within five minutes and sickling of a majority of the cells within 15 minutes. In three patients with sicklemia the response was similar; in two, the sickling was evident only after two hours.

The test is performed by adding one drop of saturated hydrogen sulfide solution to one drop of a 1:5 saline suspension of oxalated blood, and covering with a cover-slip. Exposure to air reverses or inhibits sickling; thiol antagonists such as iodoacetamide inhibit spontaneous or thiol-induced sickling. Addition of BAL or hydrogen sulfide solution to sickle cells produces a marked reduction in the sedimentation rate and eliminates rouleaux formation. 7 references. 1 table.—*B. J. Shuman.*

Sickle Cell Anemia, a Molecular Disease. *Linus Pauling, Harvey A. Itano, S. J. Singer, and Ibert C. Wells, California Institute of Technology.* Proc. Natl. Acad. Sciences 1949 Annual Meeting, Science 109: 443, Apr. 29, 1949.

The electrophoretic behavior of hemoglobin from individuals with sickle cell anemia and from normal individuals has been studied with the Tiselius apparatus. A significant difference was found between the electrophoretic mobilities of hemoglobin derived from sickle cell blood and from normal blood. The curves of mobility against pH were roughly parallel, but the isoelectric point of normal hemoglobin was lower than that of sickle cell hemoglobin for ferrohemoglobin and carbonmonoxyhemoglobin. At pH 7.0 sickle cell carbonmonoxyhemoglobin moved as a positive ion while normal carbonmonoxyhemoglobin moved as a negative ion.

It is proposed that a difference exists in the number of acidic or basic groups in the two hemoglobins, amounting to three or four such groups per molecule. This suggests that the disease has a molecular origin, and that the change in shape of the erythrocytes leading to its symptoms is the result of the difference in the properties of the molecules.

(*Considerable uncertainty has existed as to whether the basic abnormality in sickle cell anemia has been in the hemoglobin or the red cell structure. These observations implicate the hemoglobin.*—ED.)

4. Cardiovascular System

Incomplete Division of the Atrioventricular Canal with Patent Interatrial Foramen Primum (Persistent Common Atrioventricular Ostium). Report of Five Cases and Review of the Literature. *H. Milton Rogers and Jesse E. Edwards, Mayo Foundation and Mayo Clinic, Rochester, Minn.* Am. Heart J. 36:28-54, July 1948.

A detailed description is given of the clinical and pathologic changes in five cases of incomplete division of the atrioventricular canal. Four were infants who died in the first 6 months of life, the fifth was a business man who died at 36 years. In three of the cases, the degree of incomplete division was readily manifest, with a common atrioventricular canal guarded by one valve. In the remaining two cases, the once common atrioventricular canal was divided into right and left halves to a lesser degree, and other cardiac defects were present. An exposition of the embryogenesis is given.

A tabular survey is presented and analyzed of the essential features in an additional fifty cases collected from medical literature, along with the authors' five cases. Of these fifty-five cases, the median age at the time of death was 10 months. More than half of the patients had died before 1 year of age. Only five lived beyond age 30 years. The anomaly had no sex predilection.

Physiologically, the lesion acted essentially as a simple interatrial septal defect. Enlargement of the right side of the heart and widening of the pulmonary artery orifice were common associated lesions. Cyanosis was at times present at birth, but usually came later, when it signified failure of the right side of the heart, pulmonary disease or both. Cardiac murmurs, usually systolic, were frequent; they occurred in twenty-two of twenty-five cases in which adequate data were given with reference to this sign. In those case reports with an adequate history, mongolism was present in seventeen cases and its absence was recorded or could be assumed in eight cases. Bacterial endocarditis occurred in three of the fifty-five cases. 54 references. 2 tables. 10 figures.

Irreversible Cardiac Disease in Adult Life Caused by Delayed Surgical Closure of a Patent Ductus Arteriosus: Report of a Case. *T. J. Dry, S. W. Harrington and J. E. Edwards, Mayo Clinic, Rochester, Minn.* Proc. Staff Meet. Mayo Clinic, 23:267-74, June 9, 1948.

A case is presented of a 21 year old male who had been known to have an enlarged heart since the age of seven. Physical and roentgen examinations were typical of patent ductus arteriosus. Electrocardiogram showed auricular fibrillation and right axis deviation.

Following ligation of the ductus arteriosus the typical machinery murmur disappeared. Four years post-operatively there was no change in the size or shape of the heart. The patient died suddenly 4 years after ligation.

Autopsy showed the ductus closed and the heart greatly enlarged. Microscopically there was marked endocardial thickening of the left atrium and ventricle. A localized patch of intimal thickening was found opposite the former pulmonary orifice of the ductus.

This case demonstrates that ductus ligation may not eliminate the cardiac damage already produced, and emphasizes the importance of early surgical intervention. The authors believe 3 to 9 years is the preferred age for operation even in the absence of marked subjective symptoms. 1 reference. 3 figures.—*R. N. Paul.*

Fluorescein Circulation Times in Diphtheria. *Sidney Cobb and Horace L. Hodes, Ayer, Mass. and Baltimore, Md.* Pediatrics 2:303-12, September 1948.

For better evaluation of diphtheritic myocarditis, the circulation times of 35 patients have been studied by a modification of the fluorescein method of Lange and Boyd (1942). A normal control series is presented as a graph in which the circulation times are plotted against the weights of the patient. Ninety-five per cent of the determinations fall to the left of a heavy line drawn on the graph. Similar studies on 35 patients show increased circulation times for a few weeks not only in severe cases but in some patients with no auscultatory or electrocardiographic evidence of myocarditis as well. The method is deemed useful in evaluating the severity of diphtheritic myocarditis.

Seven cases of varying severity are reported in detail. The circulation time measurements in two of these suggest that the digitalis therapy they received was definitely beneficial. 4 references. 8 figures. 1 table.—*Author's abstract.*

(*Using the equation for the "normal" limit drawn by the authors, it may be stated that the circulation time by this method is normally not more than* (*body wt. lbs.* ÷ 16) + 6.6 *seconds.* (95 *per cent of* 151 *determinations on* 62 *normal patients between* 20 *and* 180 *lbs.*). *No normal patient showed a longer time on more than one determination. The authors consider their*

normal standard as tentative pending further studies. If satisfactory lower limits of normal could be established, the method would be useful in studying congenital heart disease as well, especially in showing a right-to-left shunt.—ED.)

Gangrene of Lower Extremities in Infants. Report of Two Cases. *Isaac H. Richter, and Irving A. Tainsky, Coney Island Hospital, Brooklyn, N. Y.* Am. Heart J. 36:443-46, September 1948.

Gangrene of the extremities is rare in infancy and childhood. When it occurs it usually complicates an acute infection.

This is a report of two instances. The first was a 3½ month white boy, who succumbed to "fever of unknown origin and thrombosis of both femoral arteries." The second was a 2 year old white girl with mongolism, who died of bronchopneumonia and gangrene of both feet. Severe diarrhea was present in both infants, and vomiting resulting in dehydration in one. The autopsy in the second case revealed a bland thrombus in the right dorsalis pedis and posterior tibial arteries without any involvement of the vessel walls. There was also thrombosis of a small vein. There was no abnormality of the heart and no evident sources of emboli. In the absence of arterial disease and a focus for embolization, it is presumed that the thromboses were caused by factors associated with the infections which increased the coagulability of blood. 4 references. 2 figures.

Coronary Sclerosis in Infancy. Report of Three Autopsied Cases, Two in Siblings. *Maud L. Menten and G. H. Fetterman, University of Pittsburgh, Children's Hospital of Pittsburgh, and the St. Margaret Memorial Hospital, Pittsburgh, Pa.* Am. J. Clin. Path. 18:805-10, October 1948.

This is a description of three infants under two months of age, two being siblings, in whom death was caused by coronary arteriosclerosis. The arteriosclerosis was characterized by thickening of all layers of the arterial walls and extensive deposition of calcium. In one infant the presence of a large number of eosinophils in the adventitial and outer medial cellular infiltrates lends some support to the theory of an allergic background. The occurrence of infantile arteriosclerosis in the other two who were siblings, and its probable occurrence in a previous baby of this family, would seem to implicate a congenital weakness of the elastic tissue in the arterial walls as another possible factor. 5 references. 2 figures.

5. *Chemotherapy, Drugs, Poisons, Physical Agents*

Hypocalcemia. Suggestions for Treatment. *Erika Bruck, Buffalo Children's Hospital, Buffalo, N. Y.* Exhibit, American Academy of Pediatrics Annual Meeting, Atlantic City, N. J. November 19-23, 1948.

The incidence, age distribution, blood level, causes of death, and treatment of hypocalcemia are presented as seen in nearly 200 cases over a two-

year period. Of these, 32 were newborns under one month of age. Diarrhea, rickets, and severe infections were the most common precipitating causes at all ages.

The criterion for the diagnosis was as follows:

Serum Calcium Normal Level 9.5 — 11.5 mg. per 100 cc.
Borderline Level 9.0 — 9.5 mg. per 100 cc.
Subnormal Level below 9.0 mg. per 100 cc.

Levels below 9.0 mg. per 100 cc. are associated with a pathologic response of nerves and muscles to electric and other stimuli.

The following calcium preparations are available for treatment: (1) Calcium chloride U.S.P. (1 Gm. = 270 mg. Ca and 13.5 mEq. acid); (2) Calcium gluconate U.S.P. (1 Gm. = 90 mg. Ca) comes in sterile ampules containing 10 per cent solution; (3) Calcium lactate U.S.P. (1 Gm. = 130 mg. Ca) comes in tablets of 0.3 or 0.6 Gm. (39 or 78 mg. Ca).

In patients who are able to take oral medication, calcium chloride is the drug of choice. It should be taken diluted in milk or other liquids and distributed in 4 to 5 doses over the 24 hours. The dose recommended is 0.7 — 1 Gm. $CaCl_2$ (190-270 mg. Ca.) per Kg. of body weight per day. Doses larger than 1.1 Gm. $CaCl_2$ per Kg. per day are apt to produce acidosis, particularly in babies under 3 months of age. Doses less than 0.6 Gm. $CaCl_2$ per Kg. per day may fail to raise the calcium level in the blood as rapidly as desired. The initial dose may be reduced after several days, when a nearly normal level in the serum is reached.

Contra-indications to $CaCl_2$ therapy are: (1) all diseases associated with chronic acidosis, particularly advanced renal insufficiency; (2) intestinal intolerance. Given intravenously, calcium chloride may cause severe necrosis wherever it leaks out of the vein. The intravenous use should be abandoned.

Calcium lactate is so poorly absorbed from the intestinal tract that it is inadequate for the treatment of significant hypocalcemia, even in high doses and with prolonged use. In patients who are unable to tolerate milk (e.g. allergic children) it might be used to prevent calcium deficiency.

Calcium gluconate is usually given intravenously, by rapid injection or continuous drip. Injections may be necessary as emergency treatment but if given too rapidly, heart block from temporary hypercalcemia, and even death may result. Furthermore, the injected calcium is rapidly excreted through the kidneys or shifted into the bones. The dose can never be made adequate to sustain a desired level. Not more than 1.5 cc. of the 10 per cent solution of calcium gluconate (13.5 mg. Ca) per Kg. body weight should be injected at one time. The injection should take no less than 10 to 15 minutes. The solution as it comes from the ampule should be diluted with saline in a big syringe with a small needle. Calcium gluconate in dilute solution, given as a slow continuous intravenous drip over 12 to 18 hours is probably effective when oral $CaCl_2$ is contra-indicated. Ten cc

of the 10 per cent solution of calcium gluconate (90 mg. Ca) per Kg. body weight per day is probably effective, but one-half to three-fourths of this may be adequate in some cases. Adjustment will have to be made as experience accumulates.

Calcium salts cannot be mixed with citrated plasma or blood even in highest dilutions, because clotting will follow.

Many patients will have a recurrence of hypocalcemia if treatment is continued for less than 2 weeks. However, $CaCl_2$ should not be given in full doses for more than 4 days without checking the CO_2 combining power of the serum. If the level is down the dosage of $CaCl_2$ has to be reduced. With intravenous calcium therapy, the calcium level should be checked frequently. With oral treatment it is sufficient to check it twice a week unless special indications for more frequent determinations are present.

Vitamin D should never be forgotten in the treatment of hypocalcemia. When rickets is present one may not be able to raise the calcium level in the blood to normal until enough Vitamin D has been given. 6 charts.

Acute Mercurial Poisoning by Inhalation of Metallic Vapour in an Infant. *J. S. Campbell, Kentville, Nova Scotia.* Canad. Med. A. J. 58:72-75, January 1948.

A female child of four months is described, who died two days after several hours' exposure to the vapor of one teaspoon of metallic mercury accidentally dropped on the kitchen stove. The autopsy showed generalized and pulmonary edema, dilated right ventricle, necrotic appearance of mucosa of the stomach and duodenum, and degeneration of convoluted tubules. 4 references.

The Treatment of Acute Brucellosis with Aureomycin. *M. S. Bryer, E. B. Schoenbach, R. M. Wood, and P. H. Long, Johns Hopkins University School of Medicine, Baltimore, Md.* Bull. Johns Hopkins Hosp. 84:444-60, May 1949.

Five adults with positive blood cultures for *Brucella suis* or *abortus* achieved rapid clinical response with reversal of blood cultures to normal when given aureomycin. No relapse has occurred after 2 to 8 months of follow-up. An initial oral dose of 2400 to 3000 mg. per day was given for one to eight days followed by 200 to 250 mg. every 3 hours for about 14 days. Four of the patients also received small supplemental intramuscular doses of aureomycin. Aureomycin seems an effective chemotherapeutic agent in this disease. 3 figures. 3 tables. 12 references.—*C. Whitlock, Jr.*

Preliminary Report on the Beneficial Effect of Chloromycetin in the Treatment of Typhoid Fever. *Theodore E. Woodward, Joseph E. Smadel, Herbert L. Ley, Jr., Baltimore, Md. and Washington, D. C., Richard Green and D. S. Mankikar, Kuala Lumpur, Federation of Malaya.* Ann. Int. Med. 29:131-34, July 1948.

In this study chloromycetin was given orally to 10 patients with typhoid fever. The initial dose in each case was 50 mg. per kilogram of body weight. Thereafter 0.25 Gm. was given every two hours until the temperature was normal and the same dose every three to four hours thereafter during the first five days of normal temperature. The total dose per patient averaged 19.1 Gm. given over a period of 8.1 days. The drug was well tolerated and no clinical evidences of toxicity were observed.

The mean duration of known fever prior to treatment in the 10 cases was 9.5 days. Evidence of improved general condition and lessened toxicity usually became apparent within twenty-four hours after starting treatment. The mean duration of fever after beginning chloromycetin treatment was 3.5 days. The cases were proved to have typhoid fever through isolation of Eberthella typhosa from the blood.

Two of the patients had relapses which responded promptly to a second course of chloromycetin. The organisms isolated during the relapse were as sensitive to chloromycetin as those isolated initially. 42 references. 2 tables, 2 figures.

The Use of Caronamide in Pediatrics. *T. L. Perry, Children's Hospital, Los Angeles, California.* Pediatrics 3:75-81, January 1949.

The effect of caronamide on serum penicillin levels was studied in 21 infants and children from 7 days to 12 years of age. The children received intramuscular sodium penicillin every 3 hours, and serum penicillin levels were compared before and after beginning a regime of 0.4 to 0.8 grams of caronamide per kilogram of body weight per day. The one-half hour penicillin serum levels were usually increased from 2 to 4 fold by caronamide, but the increase ranged from 0 to 16 fold. The 3 hour penicillin levels showed an average increase of 16 fold on caronamide, with the increase ranging from 2 to 128 fold. The accompanying table shows the change in serum penicillin levels following caronamide in the 8 children of this series receiving approximately 100,000 units of penicillin per Kg. per day. No correlation was found between individual serum caronamide levels and the degree of elevation of the serum penicillin level by caronamide. Attention is called to the fact that this finding is contrary to those of other investigators studying adult patients.

TABLE I.

Comparisons of serum penicillin levels in 8 children receiving approximately 100,000 of penicillin per kilogram of body weight per day divided into 3 hourly intramuscular injections before and during caronamide therapy.

CASE	WGT. IN KG.	BEFORE CARONAMIDE PENICILLIN SERUM LEVEL IN UNITS/CC.		DURING CARONAMIDE PENICILLIN SERUM LEVEL IN UNITS/CC.	
		½ *hour*	3 *hours*	½ *hour*	3 *hours*
1	10	16	1	8	2
2	12	32	0.25	64	2
3	12	8	0.25	32	1
4	4	4	0.06	16	0.5
5	3	16	0.06	64	2
6	5	128	2	64	16
7	17	16	2	128	8
8	4.5	4	0	32	2
Total		224	5.62	408	33.5
Mean		28	0.8	51	4.2
Median		16	0.25	48	2
Range		4-128	0-2	8-128	0.5-16

Newborn infants showed exceptionally high serum penicillin levels, presumably a manifestation of poor renal function in newborns.

Phenolsulfonphthalein tests on 19 of the patients during and after caronamide therapy demonstrated that the depression of tubular function by caronamide is only temporary. The only toxicity encountered was occasional nausea and vomiting, which did not necessitate stopping caronamide in any case. A false positive test for urine albumin was found on all patients receiving caronamide due to precipitation of caronamide in the urine by acid Twelve case reports are given which illustrate the type of cases in which caronamide plus penicillin has special value. The authors conclude that caronamide should be reserved for cases requiring exceptionally high penicillin serum levels. 2 tables. 15 references.—*C. Whitlock, Jr.*

Procaine Penicillin: Therapeutic Efficiency and Comparative Study of Absorption Using Various Preparations. *J. A. Robinson, H. L. Hirsh, B. Milloff and H. F. Dowling, George Washington University, Washington, D. C.* J. Lab. & Clin Med. 33:1232-40, October 1948.

At least 25 patients given different preparations of repository forms of penicillin were used for comparison of the serum penicillin levels following intramuscular injection of 300,000 units of (1) procaine penicillin in oil, (2) procaine penicillin in oil plus aluminum monostearate, and (3) procaine

penicillin in aqueous suspension. The results tabulated showed that procaine penicillin in oil and in water gives serum levels over 0.1 units per cc. for 24 hours in virtually all cases, and procaine penicillin in oil with aluminum monostearate does the same for 48 hours.

A clinical study with procaine penicillin in oil without aluminum monostearate was carried out on various acute systemic infections with dosages of 300,000 to 600,000 units once or twice a day. Results were considered similar to those obtained with penicillin in other dosage forms. Gonorrhea was treated with one injection of 300,000 units of procaine penicillin in oil plus aluminum monostearate with good results.

No systemic reaction or significant local reaction to these products was encountered in this study. An attempt to demonstrate procaine in the serum by colorimetric chemical assay in these patients was unsuccessful. — *C. Whitlock, Jr.*

(*Some authorities fear that with procaine penicillin in oil plus aluminum monostearate the amount of penicillin absorbed per unit of time is so small as to make hazardous treatment of any severe infection with this form of penicillin. Procaine pencillin in water or in oil without aluminum monostearate in a single daily dose of 300,000 to 600,000 units for adults or 13,000 units per Kg. of body weight for children has proved a satisfactory regimen for the treatment of penicillin-sensitive infections at sites in which diffusion of systematically administered penicillin is good, as, for example, pneumonia, upper respiratory infections, septicemias, and cellulitis.*

There appears to be little gain in going much above the dosage regimen outlined above for procaine penicillin, since the serum penicillin level rises little with injections of procaine penicillin above these amounts. It is better to resort to large doses of sodium penicillin with or without caronamide, in the doses recommended elsewhere in this issue, when substantially higher serum penicillin levels are desired. This latter regimen is warranted in infections relatively inaccessible to systematically administered penicillin, such as suppurative otitis media, osteomyelitis, meningitis, endocarditis, and soft tissue abscesses unsatisfactory for local treatment or in infections relatively insensitive to penicillin such as typhoid fever. Therapeutic trial on penicillin in the case of fever of unknown origin is also best conducted on such a regimen rather than with procaine penicillin, since the accessibility and sensitivity to penicillin of such an infection is unknown.

It is extremely unlikely that enough procaine to give a serious toxic reaction can reach the blood stream following the intramuscular injection of the above recommended procaine penicillin doses. More frequent or larger doses might conceivably do so. Procaine has an inhibitory effect on concomitantly administered sulfonamides, as has been shown by Maxwell Finland and other workers. That procaine penicillin in the above recommended doses will liberate enough procaine to exert such an effect seems unlikely. However, it is probably safer

not to use procaine penicillin in cases such as meningococcal meningitis when the action of the sulfonamide drug is of primary importance, and it is probably safer not to give more than the dose of procaine penicillin recommended above, when giving sulfonamide drug concomitantly in other infections.

Reactions to penicillin following procaine penicillin injections have been surprisingly few, possibly due to the presence of procaine, which is thought to have some inhibitory effect on sensitivity reactions from penicillin.

In summary then, two penicillin regimens have been developed which cover the gamut of acute bacterial infections requiring systemic penicillin therapy safely, conveniently, economically, and effectively. One is procaine penicillin injected once daily for infections responding to average amounts of penicillin; the other is large doses of sodium penicillin injected at frequent intervals with or without caronamide in infections requiring unusually large amounts of penicillin. The many other regimens for systemic penicillin treatment now in clinical use seem no more or even less advantageous than these two.—ED.)

Blood Levels of Penicillin with Oral Use of Buffered and Unbuffered Solution. *S. Q. Cohlan, J. M. Lewis, E. Seligmann, Beth Israel Hospital, New York, N. Y.* Am. J. Dis. Child. 75:15-23, January 1948.

Serum penicillin levels are determined in infants and children following equal oral doses of buffered and unbuffered penicillin. It was found that buffered penicillin gave appreciably higher serum levels than unbuffered penicillin in children, and about equal levels in infants. This difference is explained by the greater destruction of the unbuffered preparation by the acid gastric juice of children, and absence of such destruction in the less acid gastric juice of infants. In vitro experiments are described which support this hypothesis. 2 tables. 3 figures. 11 references.—*C. Whitlock, Jr.*

A Guide to the Use of Procaine Penicillin in Hospital Practice. *Gene H. Stollerman, Edward H. Roston, and Beatrice Toharsky, Mt. Sinai Hospital, New York, N. Y.* New York State J. M. 48:2501-05, Nov. 15, 1948.

Penicillin serum concentrations after single injections of procaine penicillin in 200 adult hospitalized patients are summarized in tables. It is pointed out that the penicillin serum concentration does not rise proportionately with increase in the dosage of procaine penicillin. It is also shown that no cumulative effect occurs in the serum levels after repeated injections of 300,000 to 600,000 units of procaine penicillin every 12 to 24 hours. It is concluded that 300,000 to 600,000 units of penicillin once or twice daily is adequate treatment for infections of average sensitivity and average accessibility to penicillin. 14 references. 2 tables. 1 figure.

Ulceration due to B. Pyocyaneus Treated with Streptomycin: Two Cases (*Fagedenismo a B. piocianico tratado con estreptomicina. Dos casos.*) *O. Montes, I. Gonzalea Diaz, and N. Lagos, Santiago, Chile.* Rev. chilena de pediat. 19:831-41, October 1948.

An erythematous skin lesion of the face and neck progressing to deep ulceration is described in premature twins at 2 months of life. Large doses of penicillin and sulfadiazine for 40 days were without effect. Cultures from the ulcers revealed B. pyocyaneus. Intramuscular streptomycin in doses of 50 mg. every 6 hours for 16 days and streptomycin ointment (2 mg. per Gm.) locally brought about marked improvement in 5 days with complete healing after 23 days. 20 references. 4 figures.—*A. M. Bongiovanni.*

Effect of Urea on Bactericidal Action of Sulfonamide Drugs. *A. La Londi, Austin, Texas and W. Gardner, Cleveland Clinic, Cleveland, O.* J. A. M. A. 13:406-408, Oct. 9, 1948.

Previous in vitro and in vivo observations are cited showing that urea increases the antibacterial action of sulfonamide. A discussion of the various possible explanations for this phenomenon is given.

Five chronic meningeal infections unresponsive to sulfadiazine and penicillin responded when urea was added in doses of 30 grams every four hours (or proportionally smaller doses in children) with or without discontinuing the penicillin.

It is pointed out that urea is nontoxic in the doses given. 10 references. 1 figure.—*C. Whitlock, Jr.*

6. Clinical Pathology

False Serologic Tests for Syphilis in Infants of Treated Mothers. *Dabney Moon-Adams, Bellevue Hospital, New York, N. Y.* New York State J. M. 48:1819-21, Aug. 15, 1948.

A report is given of the findings in 470 infants of treated syphilitic mothers who were examined within the first three months of life for serologic, clinical, and roentgenologic evidence of syphilis. Positive serologic tests not indicative of syphilis were found in 47.3 per cent of infants tested in the first month of life, in 16 per cent of infants tested in the second month of life, and in 1.2 per cent of infants tested in the third month of life. Negative reactions in syphilitic infants were found in five cases or 1 per cent of the total. In one of these, syphilis was probably acquired.

The duration of non-syphilitic positive serologic tests varied from twenty-four days to fourteen weeks. Of the total, 36 per cent had become negative in four weeks; 74 per cent in eight weeks; 93 per cent in twelve weeks, and 97.7

per cent in fourteen weeks. Correlation of the number of non-syphilitic positive serologic tests with the mother's treatment showed a higher percentage when the mothers were treated in the last trimester of pregnancy. Compared with statistics based on mothers treated with arsenicals and bismuth, a greater number of non-syphilitic positive serologic tests can be expected in the infants of mothers treated with penicillin.

These positive reactions of the newborn infant reversing to and remaining negative may represent a transfer of reagin from the mother's blood to the infant, or may indicate persistence of the positivity of the syphilitic fetus treated and cured in utero by the therapy given the mother during pregnancy. Neither hypothesis is susceptible of proof in any given case. 8 references. 2 tables.

7. *Endocrine System*

The Collection of Radioactive Iodine by the Human Fetal Thyroid. *Earle M. Chapman, G. W. Corner, Jr., David Robinson, and R. D. Evans, Ph.D., Boston, Mass.* J. Clin. Endocrin. 8:717-20, September 1948.

Pregnant women with organic disease which endangered their health were given tracer doses of radioactive iodine from 12 to 48 hours before surgical termination of pregnancy. The tissues from 9 fetuses ranging in age from 7 to 32 weeks have been studied for collection of radioactive iodine by the thyroid, utilizing the Geiger count. No radioactivity was demonstrated under 12 weeks of life. Increasing amounts of radioactive iodine were present after the fourteenth week. "A practical application of this knowledge lies in the use of radioactive iodine in the treatment of toxic goiter. Women up to the fourth month of pregnancy may be given therapeutic doses of radioactive iodine without retention of such radioactivity by the fetus." Histologic comparisons showed that this apparent onset of physiologic activity coincided with the appearance of follicles containing colloid. 7 references. 1 figure. 1 table.

(*This conclusion is acceptable with relation to the situation prevailing and the doses of radioactive iodine used in hyperthyroidism. The treatment of carcinoma of the thyroid with radioactive iodine is quite another matter; here the possibility of damage to the fetus, even though his gland takes up no iodine, is real because of the amount of internal radiation to which the fetus will be subjected.*—ED.)

Insufflation of Posterior Pituitary Powder in Childhood Diabetes Insipidus. Report of a Case. *Dan Feriozi and Frederick Schneider, Washington, D. C.* M. Ann. District of Columbia 17:557-58, October 1948.

A nine year old white boy is described with a typical clinical history of diabetes insipidus. Treatment with posterior pituitary powder by nasal insufflation was given. The mother first instilled 45 mg. (¾ grain) of the

powder in each nostril with the aid of a nasal insufflator on rising and at bedtime for a period of 1 week. Over 3 weeks, time the dose was gradually increased to 225 mg. daily, nasally. The patient ceased to urinate or drink water at night, and there was a cessation of bed-wetting. The previous daily intramuscular injections of pitressin were thus obviated. On one occasion when treatment was omitted because of shortage of the drug the symptoms recurred. 6 references.

8. Eye, Ear, Nose and Throat

Conduction Deafness in Children. *Frank S. Moody. Jefferson-Hillman Hospital, Birmingham, Ala.* Jefferson-Hillman Hosp. Bull. 2:94-103, July 1948.

Much alleviation of adult deafness can be attained by detection and treatment of the incipient changes during childhood. After puberty the changes leading to permanent deafness are usually irreversible.

Overgrowth of lymphoid tissue in the nasopharynx causing partial obstruction of the eustachian tubes for a number of years may produce permanent changes in the middle ear. Mucous secretions in the tympanum become myxomatous and are finally organized into fibrous tissue, interfering with the movement of the ossicles and tympanic membrane, producing loss of sound conduction across the middle ear. The best means of detecting this process in children is by testing the hearing with electric audiometer and tuning fork, examining the tympanic membrane for retraction, and inspecting the nasopharynx with the electric nasopharyngoscope to study the lymphoid tissue in relation to the eustachian tube orifices. Surgical removal of tonsils and adenoids often results in dramatic improvement of hearing, but this improvement may be lost again because of compensatory hypertrophy of the lymphoid tissue which cannot be removed in its entirety by surgical means. It is necessary to re-examine these children yearly, to keep the lymphoid tissue hypertrophy at a minimum and the eustachian tube patent.

Hearing loss in the high tones only is the first sign of progressive hearing deficiency, which usually extends octave by octave into the conversational range of tones. Every child with evidence of eustachian tube obstruction should have treatment to restore and maintain patency. Radium effectively reduces the size of the lymphoid nodules and can be easily employed even in small children.

A program is described for the detection and treatment of deafness in children. All children between the ages of 5 and 15 who come to the Department of Otolaryngology of the Jefferson-Hillman Hospital, regardless of their presenting complaint, are examined with special reference to their auditory acuity. During the first year of this work, 82 out of 301 children

examined were found to have definite conduction deafness as shown by audiograms. Two others had otosclerosis and four had perception (nerve) deafness. The chief complaint in the majority of children was frequent attacks of acute coryza accompanied by severe sore throat. Most of the group were unaware of any existing hearing loss.

The tuning fork test (Rinne) normally reveals air conduction to be approximately twice as long as bone conduction. Most cases of beginning conduction deafness have good bone conduction with perhaps moderate loss in air conduction. If the audiometric test is low, it is checked on another day and correlated with the other findings before a diagnosis of conduction deafness is made. In examining with the electric nasopharyngoscope it is the location of the lymphoid tissue in its relation to the eustachian tube orifice, and not always the amount of the tissue that is important.

When conduction deafness due to occlusion of the eustachian tubes is present one must decide whether to use surgery or radium, or both. In children with large hyperemic tonsils, enlarged cervical lymph glands, and large adenoids which obstruct the eustachian tube orifices, a tonsillectomy and adenoidectomy should be performed. If a large mass of lymphoid tissue has regrown in the nasopharynx following tonsillectomy and adenoidectomy, the mass should be removed surgically and the surgery followed by irradiation. If the recurrent lymphoid tissue is limited to the area about the orifice of the tube, a second operation may produce cicatricial stenosis of the tubal orifice, and lead to permanent injury. Radium alone is used in these cases. Adenoid tissue can grow at an alarming rate even after the most meticulous adenoidectomy. "A large number of our patients have had a considerable regrowth of adenoid tissue within eight months following the original operation."

As the result of treatment, many children with profound loss have had their hearing restored to normal. All have had a large mass of lymphoid tissue blocking their eustachian tube orifices. Practically every child in the series that has had a complete course of treatment has shown satisfactory improvement. Those who have not improved need roentgen therapy directed toward the middle ear and peripheral portion of the eustachian tube. 2 tables. 4 figures.

Problem of the Congenitally Deaf Child. *Douglas MacFarlan, Philadelphia, Pa.* J. A. M. A. 137:774-75, June 26, 1948.

The causes of deafness in young children are numerous. Only 25 per cent can be explained by heredity, and injuries at birth play an infinitesimal part. Rubella in the pregnant mother is a frequent cause. Quinine medication at parturition has been recognized as a cause. After birth, the childhood fevers may play a part in nerve and cochlear damage. Measles is the commonest

offender. Meningitis and encephalitis are occasional causes. Purulent otitis media also may destroy the infant's hearing It is usually the child's failure to develop speech about the age of 2, rather than the deafness, which is first recognized. It is highly advisable to prepare these children to enter the schools for the children with normal hearing, avoiding institutionalizing if results warrant it. Normalcy in growing up is most needed by any handicapped child. Most deaf children have some remnant of reachable, usable hearing, and means of arousing and awakening auditory attention by amplified sound are now available. The sooner treatment is started, the better.

The deaf child usually is a behavior problem. If any trace of hearing is present, he must first be taught to want to listen. The assumption may be that the child probably has some usable residual hearing. A program of training in a conditioned response is begun. Attention to sound is the primary object. The simplest conditioned response is that of raising the hand when a loud sound is presented at the ear. "This can be done by the use of an electric buzzer operating a telephone receiver, but an essential is that the receiver vibrates so loudly that it may be felt as well as heard. The parents are given such equipment and told to train the child to hold up the hand after the buzz is turned on and to drop the hand after it is turned off." Every child can be trained to raise the hand to the tactile stimulus, which is known to be unimpaired.

When the child's reactions to the training device become accurate, he can then be tested with an audiometer, and an exact record of the amount of residual hearing is obtained. Many of these children have as much as 50 to 60 per cent hearing in the speech-hearing zone. This leads one to believe that a 40 to 50 per cent loss can cause the child to become attention deaf. In a series of over 50 patients in the last two years, the author found approximately 90 per cent with usable hearing. After a hearing aid is put on even the youngest child, he is "bathed" in speech. Simple, common words are selected and a definite training program of word, phrase and sentence teaching is started. Lip reading by the child is forcibly submerged at first by the teacher who covers her lips, for these children are often natural lip readers. Lip reading is permitted later. It is important to see that tubal catarrh, adenoid hyperplasia and common head colds do not add to the deafness already present. The vestibular test should be done, preferably while the child is under light anesthesia.

(The problem of deafness in children is an ever present one. It is rather surprising to find that some of these children have from 50 to 60 per cent hearing loss as outlined by the author. Needless to say, any medicine which will increase these children's hearing is worth following up.—ED.)

9. Gastrointestinal System

Congenital Hypertrophic Pyloric Stenosis in Mother and Daughter. Report of a Case. *A. T. Henderson, R. A. Henderson and B. A. Spencer, Muncie, Indiana.* Arch. Pediat. 65: 654-56, December 1948.

Congenital hypertrophic pyloric stenosis is described in a white female and her daughter. No similar reports have been found by the authors. 7 references.

The Extraction of Secretin from the Intestine of Man: Absence of Secretin in a Case of Fibrocystic Disease of the Pancreas. *Archie H. Baggenstoss, Marschelle H. Power, and John H. Grindlay, Mayo Clinic and Foundation, Rochester, Minn.* Gastroenterology 11:208-20, August 1948.

To test the hypothesis that fibrocystic disease of the pancreas is the result of a congenital deficiency of secretin, studies were carried out to determine (1) whether or not secretin could be extracted consistently from specimens of the duodenum and small intestine at autopsy and (2) whether secretin was absent in cases of fibrocystic disease of the pancreas. The tests were done with human intestinal tissue, procured at autopsy from 18 adults and 20 children, who died from a diversity of diseases. The search for secretin in the duodenum and small intestine was performed on dogs having total pancreatic fistulae, and extractions were successful up to fourteen hours post mortem. When the specimens were preserved in a frozen state, extraction was successful as long as twelve days after death.

The presence of a pancreatic stimulant was demonstrated in all the adults and children except in extracts from the intestines of premature and newborn infants and from a single case of fibrocystic disease of the pancreas. This latter specimen was obtained from a child 16 months of age, in whom the autopsy was performed ten hours after death. It was found that by combining the extracts from 3 premature infants and also from 3 newborn infants, that active stimulation was sometimes obtainable. Secretin is probably present in the neonatal period but in small amounts.

Secretin could be extracted successfully in cases in which the illness varied in length from one day to three years. The only instance among adults in which potent secretin could not be extracted was a case of carcinoma of the uterus with intestinal obstruction. Fibrocystic disease of the pancreas seems, therefore, to be explainable in terms of congenital deficiency of secretin. Under such circumstances the thick viscid juice resulting from nervous and pancreozymin stimulation might become inspissated, thereby causing obstruction of the acini and ducts and leading to atrophy and fibrosis. The disturbances

which occasionally occur in the secretion produced by the liver and intestine conform with the secretin deficiency theory inasmuch as secretin normally stimulates also the secretion of bile and the succus entericus. 16 references. 4 tables.

10. Genitourinary System

The Roentgen Diagnosis of Diffuse Leukemic Infiltration of the Kidneys in Children. *John F. Gowdey and Edward B. D. Neuhauser, Harvard Medical School, The Infants' and Children's Hospitals of Boston, Boston, Mass.* Am. J. Roentgenol. 60:13-21, July 1948.

Of a series of 50 cases of leukemia coming to autopsy, 26 showed diffuse infiltration of the kidneys. Three cases are described in some detail.

The kidney with diffuse leukemic infiltration is enlarged, often as much as three to four times normal size, occasionally even larger. The cut surface is usually pale gray or pinkish and may show areas of hemorrhage. Microscopically, the individual nephrons are widely separated by massive cellular infiltration.

The roentgen picture following intravenous urography seems characteristic. The infiltration is usually bilateral, with symmetrical enlargement of each kidney. The renal pelves are considerably enlarged without dilatation or other evidence of obstruction; the calices and infundibula are elongated without real deformity, filling defects, displacement or irregularity of outline. Any displacement is due to attendant hepatomegaly or splenomegaly, or retroperitoneal lymphadenopathy. The roentgen appearance of the kidneys is likely to be confused with that produced by polycystic kidneys. Diodrast clearance is usually markedly diminished in polycystic kidney though normal in leukemia. Roentgen irradiation may produce diminution in the size of leukemia infiltrated kidneys. 12 references. 9 figures.

11. Growth, Puberty, Adolescence

The Acrodynia Syndrome in Young Girls. (*Le Syndrome Acrodynique Des Jeunes Fillies*). *Maurice Porot, Algiers, Algeria, Africa.* La Presse Medicale 60:709-710, Oct. 9, 1948.

The writer describes young girls having anxiety neurosis with painful kinesthetic hallucinations. They also had severe palmo-plantar vasomotor disorders with erythema, paresthesia and desquamation. The patients had experienced these disturbances previously, but more mildly. Such symptoms, not quite like those of acrodynia, seem to be related to a disturbance of the vegetative diencephalic centers. 1 reference.

12. History, Biography, Antiquities

Frederick F. Tisdall

O.B.E., M.D., F.R.C.P. (C), F.R.C.P. (Lond.)

The pediatric world lost one of its most outstanding members in the death on April 23rd of Doctor Frederick F. Tisdall, Toronto.

Dr. Tisdall was born in Clinton, Ontario, November 3rd, 1893, and was educated at Clinton Public and High Schools. He graduated from the University of Toronto Medical School in 1916, and immediately joined the Canadian Army Medical Corps and served overseas. After the war he did postgraduate work in Nutrition and Children's Diseases at Johns Hopkins Hospital, Baltimore, returning to the Hospital for Sick Children and University of Toronto in 1921.

His years of service at the Hospital for Sick Children gained him many honors. At the time of his death he was Associate Professor of Pediatrics, University of Toronto, and Physician at the Hospital for Sick Children, Toronto; also Director of Research, Department of Pediatrics and the Hospital for Sick Children. In his latter years Dr. Tisdall became intensely interested in adult nutrition. His remarkable executive ability resulted in his talents being put to use by many organizations. He was a member of the Canadian Council on Nutrition; Chairman of the Committee on Nutrition of the Canadian Medical Association; Chairman, National Nutrition Committee of the Canadian Red Cross Society; was a member of the Food and Nutrition Board, National Research Council, Washington; and during World War II was Consultant on Nutrition to the Royal Canadian Air Force, with the rank of Group Captain.

The outstanding characteristics of this man were his great energy, his good nature and kindliness. No gathering was dull when Dr. Tisdall was a member; no meeting lacked purpose; no experiment died through lack of interest as long as he was present.

Dr. Tisdall is survived by his widow and four sons. The sympathy of the pediatric world goes out to his family and to his many friends.

—J. F. McCreary

13. Infectious Diseases, Acute

Diarrhea and Dysentery in Infants and Children. *C. S. Hsiang and C. H. Yu, Medical College, National Central University, Nanking, China.* Nat. M. J. China. 34:199-216, May 1948.

This describes 206 cases of diarrhea and dysentery, exclusive of amebiasis, in infants and children under 12 years of age. Specific enteric infections were present in 86 cases and the remainder had non-specific diarrhea. In the latter group, the disease was common in the first two years of age, and from April to October. Thirty-four per cent were associated with respiratory infections; other parenteral diseases preceding the diarrhea consisted of skin infections, diphtheria, meningitis, nephritis and avitaminosis A. The common causes of the specific infectious cases were bacilli of the mannite-fermenting group (30 per cent), Salmonella (12 per cent), and Shigella (9 per cent). These occurred frequently in late summer and autumn, being absent in the first 3 months of life among those exclusively breast fed, and rare in the first year even with mixed feeding. After the first year, the incidence increased rapidly to a peak at the age of four.

Deaths occurred in 6.7 per cent of the non-specific diarrheas and in 9.3 per cent of the infectious group. 8 references. 17 tables. 7 charts.—*C. L. Kao*

A Public Health Program to Combat Influenza. *News Release, U. S. Public Health Service, Federal Security Agency, Washington, D. C.* December 24, 1948.

A plan has been developed which seeks to prevent recurrence in this country of a serious epidemic of influenza like that which occurred in 1918. The plan is part of an international program set up by the World Health Organization last year to study influenza and aid physicians and health officials in the control of the disease. An Influenza Information Center to serve as headquarters for the program in the United States has been established at the National Institutes of Health, Bethesda, Maryland.

As soon as a significant outbreak or respiratory disease suspected to be influenza has been reported in a given community, the Influenza Information Center will alert diagnostic laboratories in the region, asking them to carry out serologic tests on patients for the presence of antibody against the influenza virus. Certain laboratories will also be asked to assign to the affected community a team of investigators experienced in the technics of isolating the virus. Every new strain of virus isolated will be sent for a complete antigenic analysis to the Strain Study Center of the Influenza Commission, Army Epidemiological Board, at Long Island College of Medicine, Brooklyn, N. Y. These new strains will be considered for possible inclusion in commercial vaccines.

In the past, many cases of influenza have not been reported to health departments until outbreaks had already attained comparatively serious proportions. The laboratory identification of suspected cases has seldom been

obtained, and reported outbreaks of the disease in most instances could not be authoritatively described as caused by influenza virus. Prompt reporting by local physicians and health officers of all suspected cases of influnza is therefore essential because of the explosive character of most influenza epidemics and their exceedingly rapid spread over extensive ıreas.

The Treatment of Pneumococcal Meningitis Without Intrathecal Penicillin. *G. H. Lowrey and J. J. Quilligan, Jr. University of Michigan Medical School, Ann Arbor, Mich.* J. Pediat. 33:336-41, September 1948.

Seventeen patients with meningitis due to pneumococci were treated without intraspinal penicillin and fourteen of them recovered. Six were below 2 years of age and five were between 2 and 14 years of age. With one exception, all were treated with combined sulfadiazine and penicillin therapy. Ten of the patients had evidence of an otitis media for days or weeks before admission, four had findings of pneumonia, and three had mastoiditis. Only four had no complicating infection.

The average amount of sulfadiazine given to infants and children was 0.2 Gm. per kilogram of body weight (1.5 gr. per pound) per twenty-four hours. For the adults the average doses were 6.0 to 8.0 Gm. per day. Most of the patients were kept on this medication for periods longer than two weeks. Those who received, in addition, 320,000 to 400,000 units daily of penicillin seemed to have a more satisfactory clinical course than those given 120,000 to 160,000 units. One other patient, who did not respond to adequate systemic therapy, began to improve with the giving of penicillin into the subarachnoid space. 16 references. 2 tables.

The Treatment of Pneumococcic Meningitis With Massive Doses of Systemic Penicillin. *F. Dowling, L. Sweet, J. Robinson, W. Zellers, and H. Hirsch, George Washington and Georgetown University Medical Schools and Gallinger Municipal Hospital, Washington, D. C.* Am. J. Med. Sc. 217:149-56 February 1949.

Previous studies are cited which show that penicillin is the single most effective agent in pneumococcal meningitis, though sulfonamide is usually given too. The present accepted practice of giving intrathecal penicillin in addition to intramuscular penicillin is challenged, and the dangers and disadvantages pointed out.

In 21 adults, some with inflamed and some with noninflamed meninges, serum and spinal fluid penicillin levels were measured during a regimen of 1,000,000 units of penicillin intramuscularly, every two hours. Spinal fluid levels ranged from 0.08 to 1.25 units per cc.; serum levels taken 2 hours after the last injection ranged from 2.5 to 20 units per cc.

Eighteen adults with pneumococcal meningitis were treated with this

regimen. Ten received sulfonamides concurrently. The results are believed equal or superior to those achieved in 66 similar cases receiving intrathecal penicillin plus systemic penicillin 120,000 to 3,000,000 units daily.

Most of the deaths occurred in the patients who received concomitant sulfonamide. As the only exception to the regimen used for the treatment of pneumococcal meningitis in this study, it is suggested that a single intrathecal dose of 20,000 units of penicillin may be given to patients in extremis. Concomitant sulfonamide is deemed superfluous. 38 references. 3 tables. 2 figures.—*C. Whitlock, Jr.*

Reactions to Pertussis Vaccine. *John A. Toomey, Western Reserve University and City Hospital, Cleveland, Ohio.* J. A. M. A. 139:448-50, Feb. 12, 1949.

Because of recent reports of irreversible central nervous system reactions following the injection of pertussis vaccine, the author sent a questionnaire to a large number of pediatricians with the request that they convey whatever specific information they had on this subject. Most of the physicians who replied stated they had not seen any convulsions after injections of whooping cough vaccine. Information was received, however, with respect to at least 38 well authenticated cases. These children were reported from various parts of the United States, most being in the east and midwest. There was no common denominator with respect to manufacture, type of vaccine or number of injections. A fair percentage had received fluid toxoid. In most of these cases the recovery was complete but two had bad reactions and died, four had subsequent convulsions, four were simultaneously ill with other diseases and five had convulsions prior to injection. One physician, a neurologist, reported having seen 12 children all with irreversible brain changes. It is noteworthy that no two of the children had exhibited these untoward symptoms after doses taken from the same vial.

The following recommendations are made:

"No child should receive injections of pertussis vaccine in large amounts (40 billion organisms, double strength) who has (a) any family history of convulsions, (b) a present history of convulsions or (c) illness of any kind, especially if it pertains in any way to the central nervous system. If there is any doubt, the dosage should be decreased. A report should be made of every apparent reaction and complete data should be kept by the physician. Perhaps the United States Public Health Service should standardize vaccine not only for potency, but for aging. There are not enough reported aftermath reactions to discontinue the use of vaccine."

(This survey by Dr. Toomey makes it clear that convulsions following whooping cough vaccine do sometimes occur, and that a fair percentage can permanently damage the brain. Several possibilities may explain the phenomenon. It is conceivable that the vaccine as given contains some neurotropic virus or toxin, perhaps from the pertussis organism itself. If this were so, however, the incidence of convulsions or encephalitis would be much higher,

particularly with respect to inoculees from the same vial or batch of vaccine. Accidental entry of the vaccine into a vein may be the mechanism at fault. The most likely explanation, in the light of present knowledge, is that there exists a constitutional factor predisposing to convulsions in the children who exhibit this reaction. Among the cases in Toomey's series and in the earlier series reported by Byers and Moll there were a few whose close relatives had epilepsy or a tendency to convulsions. That is to say, the immediate response in these children may be a generalized toxic reaction with fever and the convulsions. Encephalopathy results later from the trigger effect of the fever upon the irritable nervous system. The mechanism behind the convulsions is the same as that which leads to convulsions at the onset of such febrile diseases as acute tonsillitis, pyelitis, and similar infections. It is this probability which lies behind the suggestion of Faber that the National Institute of Health or some other responsible body test every batch of commercial whooping cough vaccine for the presence of pyrogens and discard all which may contain any.

The number of convulsive attacks and subsequent encephalopathy following whooping cough vaccine is higher than Toomey's survey has uncovered. The editor knows of two such instances, neither of which has been included in this series. Nevertheless, the seriousness of whooping cough and the frequency of cerebral and other permanent complications which may follow an attack are sufficiently great to warrant the continuance of generalized administration of whooping cough vaccine. The practitioner should proceed with caution or perhaps even discontinue the injections entirely whenever a child has a severe constitutional reaction to the first or second injection of whooping cough vaccine. The available data make it clear that no one type of vaccine is more or less likely to induce severe clinical reactions than any other type.—ED).

Pertussis in Infancy. *Nicholas Rizzo, Infants' and Children's Hospitals, Boston, Mass.,* J. Pediat. 33:300-312, Sept. 1948.

The author presents an analysis of 137 cases of pertussis in infants under 2 years of age of whom 45 were treated with pertussis hyperimmune serum. It was not found possible to prove or disprove the value of serum treatment, although the mortality rate was shown to be less since its inception. However, improvements in supportive therapy and the use of sulfonamides for some of the complications may have been responsible for this reduction.

No study was made of the prophylactic use of pertussis hyperimmune serum although its efficacy has already been clearly established. 25 references. 10 tables. 2 figures.—*R. N. Paul.*

Streptomycin in the Treatment of Pertussis. *H. Leichenger and A. Schultz, Cook County Hospital, Chicago, Ill.* J. Pediat. 33:552-55, November 1948.

Previous in vitro and animal studies are cited showing streptomycin to be effective against H. Pertussis.

Early cases of pertussis were assigned in rotation to one of three groups. Group I patients received 1 Gm. of streptomycin daily by aerosol divided into

three-hour doses for one week. Group II received a similar course of streptomycin intramuscularly. Group III received only symptomatic treatment. The results are tabulated below:

	Average number of paroxysms per day.		Average duration in seconds of paroxysms per day.		Number of children
	Before Treatment	After treatment	Before Treatment	After treatment	
Group I	14	4.3	30.6	20.9	8
Group II	15.8	6.0	42.0	25.1	8
Group III	13.4	8.6	37.1	38.4	7

One patient died in the control group.

It is concluded that streptomycin, especially by aerosol, is an effective therapeutic agent in the treatment of pertussis. No comparison of efficacy of streptomycin and hyperimmune serum was attempted. 4 tables. 5 references.—*C. Whitlock, Jr.*

(*The difficulty of evaluating the results of treatment in pertussis make it desirable to have additional cases treated by this promising method before conclusions can be drawn.*—ED.)

Streptomycin Therapy for Pertussis. *V. H. Gordon and P. J. Almaden, University of Arkansas School of Medicine, Little Rock, Ark.* J. Pediat. 34:279, March 1949.

The course of pertussis in 27 severely ill children treated with streptomycin is compared with that of 28 comparable cases not so treated. The effect of streptomycin was definitely favorable, the fatality rate being 7.4 per cent in the treated group and 39.3 per cent in the control group. The dosage employed was 25 mg. per lb. of body weight per day divided equally and given every three hours intramuscularly for an average of 7 days. It is concluded that children severely ill with pertussis should be hospitalized and receive streptomycin in addition to hyperimmune serum whenever possible. 3 tables. 17 references.—*C. Whitlock Jr.*

Primary Pneumonitis in Infancy. *John M. Adams, University of Minnesota Medical School, Minneapolis Minn.* J. A. M. A. 138:1142-44, Dec. 18, 1948.

Attention is directed to what is viewed as a specific variety of primary pneumonitis in infants. The ailment can range in severity from minimal to intense. There may be little or no evidence of infection in the lower respiratory tract as determined by usual methods. Morbidity and mortality have been extremely high in prematurely born babies as contrasted with normal full term infants. The disease may be very mild or even latent in older children and adults.

In the typical sporadic case a history of mild disease of the respiratory tract in one or both of the parents is frequently elicited. The onset in the

baby is rather abrupt, and at times the pulmonary symptoms may be the first observed. Sneezing and cough are the first symptoms. Fever is usually slight. The more severely ill cases have marked dyspnea with retraction of the soft parts of the chest and some cyanosis. These signs may be severe, occurring in attacks usually at the time of handling or feeding. The exudate in the pharynx is abundant, whitish, thick and tenacious. Rales may be heard over the lung fields on careful examination. Roentgenogram of the lungs reveals diffuse shadows which are bronchial in distribution and usually widespread, but may be confined to a single lobe of the lung.

The diagnosis is made by the symptom pattern and by the rather characteristic shadows seen in roentgenograms of the lungs. The diaphragms of the patient are depressed and there is evidence of emphysema. The white blood cell count is usually normal or only slightly elevated, with a predominance of lymphocytes. Pharyngeal smears in the acute stage of the disease reveal a great predominance of epithelial cells which contain cytoplasmic inclusion bodies. When stained with hematoxylin and eosin in the routine manner, the inclusion bodies are bright red or eosinophilic. There is a clear zone or halo about the inclusion bodies; they lie next to the nucleus of the cell and frequently indent it slightly.

Treatment is largely symptomatic. Continuous oxygen has been beneficial to the infants with involvement of the lower respiratory tract. Sulfonamide drugs and antibiotics have not been very useful, though sometimes employed to combat possible bacterial complications. Many postmortem studies have revealed destruction and proliferation of bronchial and bronchiolar epithelium with peribronchial infiltration of mononuclear cells Typical cytoplasmic inclusion bodies are found in the epithelial structures of the pulmonary tree. This includes the nasal, pharyngeal, tracheal, bronchial and alveolar tissues. This finding of inclusion bodies depends for its significance upon correlation with clinical evidence of a characteristic disease, and whether or not they occur in large numbers, exclusive of other findings, in carefully prepared pharyngeal smears. The age of the patient probably plays a role in the occurrence of these bodies since they have not been described in lung sections from adults dying of nonbacterial pneumonia. 2 references. 2 figures.

A Proposed Provisional Definition of Poliomyelitis Virus. *Committee on Nomenclature of the National Foundation for Infantile Paralysis.* Science 108:701-05, Dec. 24, 1948.

SUMMARY AND RECOMMENDATIONS

"(1) The term poliomyelitis virus should be used to designate strains of the agent originally described as the cause of poliomyelitis in man and only

these. It is identified by the characteristic experimental disease in the monkey, by the character and distribution of histological lesions in the spinal cord and brain of infected primates, by its host range, and by its immunological properties.

"(2) Strains of poliomyelitis virus have been distinguished by immunological methods. With the exception of the Lansing group, they are as yet poorly defined. Some strains in this group have special properties of infecting cotton rats, mice, and hamsters as well as primates. Human sera may contain antibodies to these strains. Because they also satisfy all other identifying criteria, their inclusion as examples of true poliomyelitis virus is justified.

"(3) Certain encephalomyelitis viruses of mice, such as Theiler's TO, FA, and GD VII strains, have been termed 'mouse poliomyelitis' by some. This term should be discontinued and Theiler's original designation of spontaneous mouse encephalomyelitis used to describe these viruses.

"(4) Other viruses which produce paralysis and neuronal lesions in the anterior horns of the spinal cord in experimental animals, but which do not otherwise satisfy the criteria set down for poliomyelitis virus, should not be called 'poliomyelitis virus,' 'mouse poliomyelitis virus,' or 'poliomyelitis-like virus'." 11 references.

(Ignorance or confusion obtains in the minds of most physicians, including those actually working in the field, with respect to understanding the many viruses which are known or suspected to be causative agents of poliomyelitis. Some of these viruses, such as Theiler's TO, FA and GD VII, and MM, EMC and Columbia SK, give rise to poliomyelitis-like diseases in animals. None of these has been shown to produce poliomyelitis in man. It is the opinion of the Committee that the time is not ripe for setting up a broad genetic group of animal and poliomyelitis viruses, but that the term poliomyelitis virus be restricted to strains recovered from the disease in man. The recommendations are not presented as official standards, but more modestly as the expression of opinion of a group of experts. The members of the Committee were: C. Armstrong, D. Bodian, T. Francis, Jr., A. B. Sabin, and J. R. Paul. All four items quoted above were approved by a group made up of many of the leading investigators in the field, namely R. Thompson, S. O. Levinson, A. J. Shaughnessy, H. A. Howe, J. H. S. Gear, G. Dalldorf, L. Aycock, P. R. Lépine, I. M. Morgan, R. Ward, C. W. Jungeblut, J. L. Melnick, S. Gard, T. M. Rivers, H. M. Weaver, and T. E. Boyd. The date of this action was July 14, 1948, during the First International Conference on Poliomyelitis in New York City.

Special interest attaches itself to the correct status of MM virus, mentioned in the Committee's list of viruses not truly poliomyelitic, because of the fact that the effectiveness of Darvisul, a sulfathiazole compound which has recently attracted attention as a possible antipoliomyelitic agent, has been proved only against the MM virus. According to the original communication of Jungeblut and Dalldorf (Am. J. Pub. Health, 33:169, 1943) this virus was originally recovered, by inoculation into a rhesus monkey, from the medulla and cord of a patient with poliomyelitis diagnosed on "clinical and patho-

logical" grounds. From the rhesus cord the virus was passed into a hamster and thence into cotton rats, albino mice and other hamsters, but after passage into the small animals proved to be no longer pathogenic for rhesus. Neutralization tests of murine material showed a close relationship with Theiler's and murine SK viruses but not with monkey-adapted or human strains. More recently, it has been further shown that MM, unlike true poliomyelitic virus, is blood-borne. The possibility of accidental contamination with latent or laboratory viruses is mentioned in the original communication and this now appears to be highly probable. Present opinion is that MM is not a true poliomyelitis virus, and that results of the tests of Darvisul against MM cannot be regarded as supporting the view that the drug might be useful in human poliomyelitis.—ED.)

A New Method in the Management of Acute Anterior Poliomyelitis. *Emil Smith, David J. Graubard, Norman Goldstein, and William Bikoff, Kingston Avenue Hospital for Communicable Diseases, Brooklyn, N. Y.* New York State J. Med. 48:2608-11, Dec. 1, 1948.

Seventy-nine cases of acute anterior poliomyelitis were treated with intravenous infusions of procaine, by administration of Priscol or by diethylaminoethanol. The investigation was originally undertaken to determine the efficacy of procaine hydrochloride administered intravenously in cases of acute poliomyelitis, but it was thought worthwhile also to investigate Priscol hydrochloride (2-benzyl-4, 5 imidazoline hydrochloride) because of its known sympatholytic action, and diethylaminoethanol hydrochloride because of its procaine-like action as an analgesic. The underlying purpose was to investigate these substances as possible alleviators of the peripheral vasospasm and muscle pain and spasm during the acute stages of the disease. The authors hypothesize that the involvement of the sympathetic components of the spinal cord are the incitants of these troublesome symptoms. Priscol hydrochloride was given according to age. Adolescents and adults received 50 milligrams intamuscularly every 4 hours for 48 hours and were then placed on a similar dose orally. Children over five years of age were given 25 milligrams intramuscularly every 4 hours for 48 hours and then the same dose orally. Children unable to take the tablets orally were given elixir of Priscol. Children under 5 years of age received an initial dose of 10 milligrams of elixir of Priscol* Each succeeding dose was increased every 4 hours by 10 milligrams until flushing or "goose-flesh" was noted, manifestations which were taken to indicate the optimal dose for the patient.

The procaine hydrochloride was injected intravenously, calculated on the basis of 4 mg. per Kg. of body weight, as 0.1 per cent (1:1000) solution in isotonic saline. Infusions were given on a symptomatic basis.

Of diethylaminoethanol hydrochloride, one or two grams in tablet form were taken orally in 4 divided doses daily. Four cases were given procaine hydrochloride; 73 cases were treated with Priscol hydrochloride and two with diethylaminoethanol.

Acute pain was relieved in all cases within a period of 20 minutes to 8 hours. Procaine hydrochloride gave the quickest and diethylaminoethanol the slowest response. Increasing relief of pain was obtained with successive doses to the point of complete relief. No deleterious side reactions were noted from the use of the drugs. Five per cent of the patients receiving Priscol in the febrile stage of the disease developed nausea and vomiting. When this reaction occurred, intravenous infusions of 10 per cent glucose in isotonic saline were given in addition. All nausea and vomiting ceased when the patient became afebrile. None exhibited diarrhea. The majority had unusually brief constipation periods.

Complete relief of pain was achieved in one to fourteen days. In no case did the acute pain persist for more than 24 hours. Some patients still had deep muscle tenderness upon pressure or mild skin or subcutaneous hyperesthesia at the time of transfer, but were sufficiently improved to undergo orthopedic after-care. Repeated blood counts and urinalyses revealed no change due to these drugs.

These results are presented as being a preliminary study. 20 references. 5 case reports.

* *The Elixir of Priscol was especially prepared for this study and is not now available commercially. Inquiries may be addressed to Ciba Pharmaceutical Products, Inc., Summit, New Jersey.*
(*See Editorial Note following next abstract*).

The Role of the Sympathetic Nervous System in Acute Poliomyelitis. *Emil Smith, Philip Rosenblatt and Andrew R. Limauro, Kingston Avenue Hospital for Communicable Disease, Brooklyn, N. Y.* J. Pediat. 34:1-11, January 1949.

In patients with acute poliomyelitis the authors have encountered Horner's syndrome, spasm of the pulmonary blood vessels with dilatation and irregularity of the right side of the heart, pylorospasm, constipation or diarrhea, intestinal obstruction secondary to rectal spasm, retention or incontinence of urine, and angioparesis or spasm of the blood vessels of the skin. Involvement of the skin vessels is indicated by profuse sweating; tache spinale which is slow to fade; skin eruptions which are vesicular, morbiliform, or scarlatinaform; and angiospasm as evidenced by the manner in which the Schick test on a paralysed upper extremity may manifest itself within twelve to twenty-four hours in the form of intense redness with vesiculation, or even a single large bulla. Healing is slow, and takes as long as two to three months. This indolence is attributed to angiospasm, which diminishes the blood supply to the tested area and hence fails to remove the toxin causing the sloughing area.

Histopathologic studies give evidence that invasion and inflammation occur in the lateral horn of the spinal cord in which the sympathetic nerves have their origin, and in the cervical sympathetic chains. From such anatomic observations the authors explain the functional insufficiency of the sympathetic nervous system as manifested in the clinical observations noted. The observa-

tions of Collens, Foster and West (1947) are cited, with respect to fifteen convalescing poliomyelitis patients treated with paravertebral sympathetic block. Oscillometric recordings at the ankles were increased after the injections. Pain, muscle spasm and tenderness were either relieved or alleviated completely. 12 references. 1 table. 2 figures.

(*The not infrequent occurrence of lesions and clinical disturbances of the autonomic system in poliomyelitis has long been recognized, but general opinion holds that pain in this disease usually originates in the sensory (exteroceptive), rather than in the autonomic apparatus. It is by no means clear that the authors selected only patients with manifest sympathetic disturbances for the trial of "Priscol", the drug used in 73 out of their 79 cases. Relief of pain in one to fourteen days (at an unstated period after onset of the disease) proves nothing since pain frequently subsides spontaneously within the same period. Control observations are not cited.*

The medical profession has the right to demand that the proponents of any new method of treatment submit convincing proofs of its efficacy. The effect of intravenous procaine in 4 cases (a route of dubious safety for this drug) may well have been simple analgesia without relevance to the sympathetic system. Until many controlled series of cases are carefully studied, it seems wise to retain a healthy skepticism with respect to the treatment as here outlined.—ED.)

Q Fever. History and Present Status. *R. E. Dyer, U. S. Public Health Service, Bethesda, Md.* Am. J. Pub. Health 39:471-76, April 1949.

In 1937, cases of a peculiar infection due to a rickettsia were described simultaneously in Australia and the United States. The infectious agents though isolated on opposite sides of the globe were soon shown to be identical. In 1940 the disease was found to produce a pneumonitis which in many instances resembled a typical pneumonia. Endemic areas have since been found in Australia, the United States, various countries of the Mediterranean area, Panama, and Switzerland. The name "Q" fever was coined by the Australian investigator Derrick in 1937 and stands simply for "Query."

The first cases reported were among workers in an abbatoir. There was no evidence which would suggest person-to-person transmission. Other cases were soon identified in Australia by serologic methods.

Derrick succeeded in transferring the infectious agent of Q fever from some of his cases to guinea pigs by blood inoculation, and later to other animals. Burnet found that the etiologic agent passed through bacterial filters, and discovered rickettsia-like bodies in the spleens of infected mice. He was able to grow these organisms on the chorio-allantoic membrane of the developing chick embryo.

Certain differences distinguish the etiologic agent of Q fever from all the other rickettsiae. It does not develop agglutinins for any known strain of proteus, it readily passes bacterial filters and shows greater resistance to physical and chemical agents. Hence the name *Coxiella burneti* for the

organism observed by Burnet. By 1940 the infectious agent had been isolated from naturally infected bandicoots and ticks in Australia. A rickettsia had been isolated from ticks in Montana and, by accidental laboratory infection, had proved to be infectious for human beings. These two rickettsiae have been shown to have at least a very close relationship, being serologically and immunologically identical. Convincing epidemiologic evidence incriminating arthropods as transmitters to human beings, is, however, lacking.

A number of epidemics have been described in the past eight years in various parts of the world. In the United States no evidence of endemicity was obtained until 1946 when outbreaks were recognized among abbattoir and stockyard workers in Amarillo, Tex., and Chicago, Ill. In these outbreaks as in most others the most likely mode of infection seemed to be the inhalation of, or contact with, infected material, most probably from infected animals. In 1947, cases were detected in Los Angeles County, California. Practically all of these had been in contact with cows, and some of the cows were found to possess serum antibodies against *C. burneti*. This organism has been found in raw milk produced in the Los Angeles area, but the importance of infected milk in the transmission to man is not yet determined. Pasteurization eliminates most if not all of the demonstrable rickettsiae in milk. Contact with livestock by reason of occupation or residence seems, at present, to be a more important factor. Work is now being done in the preparation of vaccines.

Infected cows, sheep and goats, the milk of these animals, wild animals, and a wide variety of ticks are potential sources of Q fever. Epidemiologic studies in abattoir workers, laboratory workers, dairy workers, and residents of dairy areas indicate that an important route of transfer to man is through droplet infection and dust. 23 references.

Rickettsialpox. *Harry M. Rose, Presbyterian Hospital and College of Physicians and Surgeons, Columbia University, New York City, N. Y.* New York State J. Med. 48:2266-70, Oct. 15, 1948.

Rickettsialpox is now of common occurrence in all parts of New York City, except Staten Island. More than 350 cases have been formally reported to the Department of Health since the spring of 1946, and many others have probably passed unrecognized, especially those of mild or atypical character. An analysis is given of the findings in 17 hospitalized cases, aged 2 to 56 years.

In 15 of the 17 patients a primary lesion could be identified with certainty. These consisted of areas of erythema and induration from 1.0 to 2.5 cm. in diameter. Two had a large, central vesicle containing cloudy fluid. In others the site of the original vesicle was represented by a central dark brown or blackish, crusted area. These lesions were on the legs, arms, neck, face,

back or abdomen. Three patients had two primary lesions. In practically every instance the lymph nodes draining the area or areas where the primary lesions were situated were enlarged and slightly tender. There was never any clinical lymphangitis.

In the majority of cases the rash appeared within six days after the onset of fever. The individual lesions usually consisted of erythematous maculopapular lesions ranging from 2 to 8 mm. in diameter. They were discrete and generally distributed over the body surface, including the face, and in three cases were on the palms and soles. Most lesions developed vesiculation. The eruption was never pruritic. Following its disappearance a few spots of brownish pigmentation remained, but with no residual scarring. In five of the 17 cases an enanthem was present, the lesions resembling those on the body surface. The enanthem was present for less than 48 hours in three patients and may be missed unless carefully searched daily.

Constitutional symptoms were chiefly fever, headache, chills or chilly sensations, and backache or general muscular aching. These symptoms appeared two to seven days after the appearance of the primary lesion. The fever curve was of the remittent type and fell to normal by lysis, generally within a week. Headache was a very prominent feature and was usually frontal. Complaints of chilliness were common and nine of the 17 patients had shaking chills with drenching sweats. Backache and general muscular aching were quite severe. Other occasional symptoms were pain and stiffness of the neck, photophobia, nausea and vomiting, cough, and sore throat. The spleen was palpable at the height of the disease in three patients, and a mild conjunctivitis appeared in three others. Nearly all showed a moderate or marked leukopenia during the acute phase of the illness. Only three had counts in excess of 7,000. In twelve of the patients the white count and differential smear were normal. In five, however, the smears showed a number of abnormal leukocytes — large mononuclear cells with vacuolated cytoplasm — resembling the peculiar cells observed in infectious mononucleosis. These abnormal lymphocytes did not persist in the blood and were present for only a day or two. Tests for heterophile antibody never showed a significant titer of sheep cell agglutinins, either during the acute illness or in convalescence.

Weil-Felix agglutination tests with Proteus OX19 and OXK with 13 patients were negative.

From seven to nine patients R. akari was isolated by mouse inoculation, and from one of these patients the organism was also cultivated directly in chick embyros. If mice are not immediately available, the blood may be frozen and stored in solid carbon dioxide. Rickettsiae have been isolated from such frozen specimens at intervals up to six months after storage. From infected mice on the first or later passages, rickettsiae may be readily transferred to chick embryos, and may be maintained indefinitely in chick embryos by serial passage.

Blood specimens were obtained for complement fixation during the acute phase of the illness and again during convalescence, two to seven weeks later.

With every case there occurred a significant rise in rickettsial antibody in the convalescent serum. A considerable degree of cross reaction was observed in most cases with the rickettsialpox and spotted fever antigens, indicating a close antigenic relationship between R. akari and R. rickettsii. Minor cross reactions were frequently observed with R. mooseri, the agent of murine typhus.

Rickettsialpox has been most frequently confused with chickenpox. The differential diagnosis may not be easy. The most important points are the presence of a primary lesion and the fact that the exanthem develops as a single crop of cutaneous lesions, whereas in chickenpox the eruption appears as successive crops of vesicles. Infectious mononucleosis may be suspected. Other rickettsial infections to be distinguished are murine typhus and Rocky Mountain spotted fever. In neither is there a primary lesion or vesicular rash, and in both the Weil-Felix test with Proteus OX19 is usually positive. One of these cases of rickettsialpox, however, had no detectable primary lesion and exhibited a nonvesicular rash indistinguishable from murine typhus. The definite diagnosis of rickettsialpox rests on demonstrating the specific immune response, or recovery of the causative agent. 10 references. 1 table.

Ritter's Disease. *Ji Chen and Tseng-Yung Shen, St. John's University Medical School and St. Luke's and St. Elizabeth's Hospital, Shanghai, China.* Chinese M. J. 66:356-58, July 1948.

A case of Ritter's disease or dermatitis exfoliativa neonatorum was treated with vitamins and penicillin, resulting in a good recovery. The infant was admitted at one month with vesicles and bullae over the whole body, superimposed on an erythematous background. The vesicles had been present for 5 days, first appearing on face and neck and spreading rapidly downwards. Certain areas showed denudation of the skin. Even slight friction would result in denudation of vesicles or even of apparently healthy skin. The temperature ranged from 103 to 107 F. Treatment consisted of penicillin 5,000 units intramuscularly every 3 hours for 4 days and thiamin 5 mg., riboflavin 1 mg., ascorbic acid 100 mg. and niacin 50 mg. daily for 9 days. 7 references. 2 figures.—*C. L. Kao.*

Desirability of the Routine Use of Tetanus Toxoid. *Edward Press, Regional Medical Director, Chicago Regional Office, United States Children's Bureau, Federal Security Agency, Chicago, Ill.* N. England J. M. 239:50-56, July 8, 1948.

The author has surveyed the present status of active immunization against tetanus in order to determine whether such immunization should be limited to special groups or be administered routinely to all children or adults.

In the last twenty to thirty years there has been little, if any, change in the over-all case mortality. The best rate in any statistically significant series has been about 35 per cent, and the average is 44.7 per cent. About 50 per cent of all injuries leading to tetanus in the civilian population are exceedingly trivial or completely unknown. Tetanus spores are widely distributed and are found more frequently in feces of humans than of horses.

The mere presence of tetanus spores in a wound is not sufficient to cause the disease. Cases of tetanus are much fewer than the number of injuries capable of resulting in tetanus. Several possible explanations for this are mentioned, including evidence for the existence of a natural immunity.

Statistical evidence indicates that less than 20 per cent of the cases of tetanus which occur in the United States are reported. There were at least 910 deaths due to tetanus in 1940. This compares with 1457 due to diphtheria, 1378 to typhoid fever and 706 to measles.

Tetanus antitoxin when given prophylactically frequently fails. About 7 per cent of civilian and over 50 per cent of military cases developed in spite of its use. "Tetanus antitoxin when given at the time of an injury is usually effective in preventing tetanus. However, to ensure success it is necessary to continue administering the antitoxin every ten to fourteen days until complete healing has taken place. This is usually not done, and in the majority of cases only a single dose is given, often resulting in a false sense of security."

It is concluded that tetanus toxoid should be given to all children, preferably along with diphtheria and pertussis immunization. Adults with increased accident hazards, such as manual laborers in both rural and urban areas, should also be immunized. 35 references. 6 tables.

Typhosus Meningitis in Children. *Yung-En Kao, National Kweiyang Medical College, Kweichow, China.* Chinese M. J. 66:83-4, February 1948.

A 3-year-old child was admitted with fretfulness, mental depression and paralysis of the left side of the body for 2 weeks. She exhibited partial deafness in both ears and marked muscular weakness of the left extremities. The white count varied from 10,000 to 14,600 with polys 68 to 84 per cent. B. typhosus was isolated persistently from the spinal fluid. Sulfanilamide was given for six days. The child died at the end of the third week of the disease.—*C. L. Kao.*

Generalized Vaccinia. *Harry S. Mustard, Jr. and Philip W. Hedrick, Willard Parker Hospital for Contagious Diseases, New York, N. Y.* J. Pediat. 33:281-94, September 1948.

Fifteen cases of generalized vaccinia are described and discussed. Ten of these were 2 years old or under; two were between 2 and 6 years; and three were adults. Eleven had infantile atopic eczema; one was receiving antisyphilitic therapy and had arsenical dermatitis; two had concurrent dermatoses, eczemoid in character; and in one the vaccinia was superimposed on chickenpox. It is pointed out parenthetically that several hundred patients have been vaccinated against smallpox, in the usual manner, at Willard Parker Hospital while ill with chickenpox, and so far as is known only this one developed generalized vaccinia lesions.

These experiences demonstrate that subjects with eczema or burns should not be vaccinated, nor should they remain in the same household with those recently vaccinated. It would seem wise to perform vaccination during the first few months of life before the onset of most allergic skin conditions and before the infant is able to scratch. In the presence of eczema in a member of

the household, a vaccinated individual should live apart from the eczematous individual until completion of the vaccination reaction. The following treatment is recommended for patients with generalized vaccinia lesions: Suppression and prevention of secondary infection by parenteral penicillin and saline compresses, or penicillin ointment locally as indicated. Prevention of further allergic reactions by removing from the diet the usual allergenic foods, including milk, orange juice, chocolate, wheat, and egg. Maintenance of adequate hydration and proper balance of the body electroytes. Prevention of further autoinoculation through restraint from scratching. Placing the infant in such a position as to minimize friction between the bed and the most extensively involved area. Elbow splints are applied. Fingernails and toenails are clipped and the hands covered with white cotton stockings. Application of protective dressings with penicillin ointment. An eczema jacket may be used. 16 references. 1 table. 2 figures.

(*Because no specific treatment is known which will influence vaccinia virus infections, management should consist of bland local therapy and parenteral fluids as needed. In our experience, penicillin has been of little value and should not be used locally. As the authors indicate, prevention is the best treatment. The mortality rate from eczema vaccinatum is sufficiently high to absolutely interdict vaccination for smallpox in the presence of eczematous lesions of the skin.*—ED.)

14. *Infectious Diseases, Chronic*

Childhood Mortality from Rheumatic Fever and Heart Diseases. A Statistical-Epidemiological Investigation into Differential Mortality by Age, Race and Sex in the United States, its Geographic Divisions, and Individual States. *George Wolff, Children's Bureau, Social Security Administration, Federal Security Agency.* Children's Bureau Pub. 322:1-63, January 1948.

A statistical survey of deaths from rheumatic fever and heart diseases in childhood, for the 3-year period 1939-41, based on material obtained from the Vital Statistics publications of the United States Bureau of the Census, has been prepared in the Children's Bureau. During this three year period, 12,037 deaths from heart diseases (all forms) and 2,538 deaths from acute rheumatic fever were counted in persons under 20 years of age; altogether 14,575 deaths. Considering that in the age group under 5 years most fatal heart diseases are not of rheumatic origin and that in later childhood (5 through 19 years) some deaths from heart diseases (perhaps 10 per cent) may also not be of rheumatic etiology, there remains a minimum of approximately 12,000 deaths caused by acute rheumatic fever and its aftereffects in the years of childhood.

By comparing the six leading causes of death in school age and youth (5-9, 10-14, and 15-19 years) it was found that, disregarding accidents, with increasing age of the children mortality from acute rheumatic fever plus diseases of the heart holds an increasingly high place among fatal diseases in the white population. In the nonwhite by far the greatest killer is still tuberculosis, especially for the girls entering childbearing age. But it is remarkable

also that the same nonwhite girls, 15-19 years old, suffer a decidedly higher mortality from heart diseases than the nonwhite boys of this age.

The white children, in the three age groups from 5 through 19 years, exhibit a very distinct decrease in mortality from acute rheumatic fever and from diseases of the heart. But for the nonwhite children no consistent downward trend is visible, except in the oldest age group 15-19 years. Disregarding the group of preschool children under 5 years, we observe that with increasing age, in both sexes and both racial groups, there is a distinct increase in the death rates for chronic rheumatic diseases of the heart and heart diseases (all forms).

The race differential in the country as a whole is demonstrated by the ratios of the death rates, nonwhite to white. They show that in almost all age-sex groups and for all three listed causes the mortality rates of the nonwhite exceed those of the white children. The consistent difference tends to show that rheumatic fever and heart diseases are unfavorably influenced by adverse socio-economic conditions.

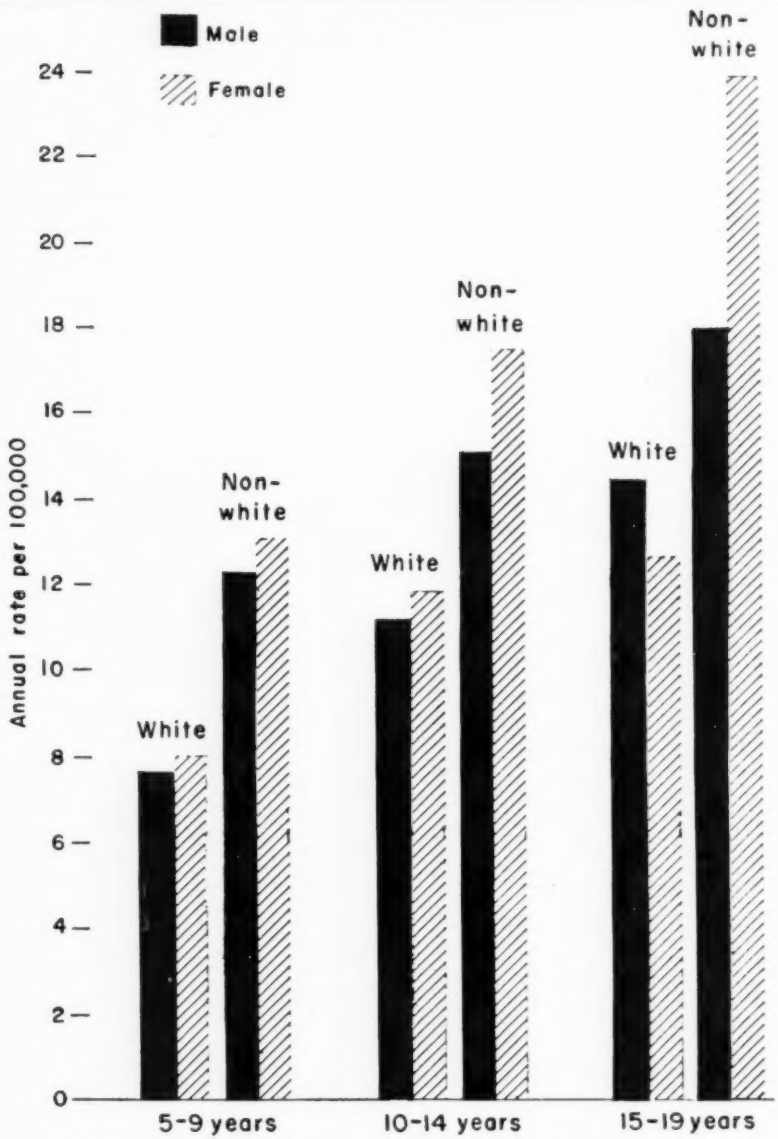
Sex differential ratios reveal that there is little consistent sex difference for mortality from rheumatic diseases in the total United States except in the age group of the older children 15-19 years. In this age group the nonwhite females show distinctly higher mortality rates than the nonwhite males while in the white group the rate for females is lower than for males.

Mortality from acute rheumatic fever and diseases of the heart varies among the geographic division of the United States. In general, for both white and nonwhite children, the death rates for acute rheumatic fever plus heart diseases are below average in the South while in the Northeast, especially in the Middle Atlantic division, they are significantly above average. In the Pacific division the death rates are as low as in the South and significantly below the country's average while in the Mountain division they are exceptionally high for the white children in all age groups.

This geographic tendency becomes still more evident when the race distribution of white and nonwhite children is kept constant by adjusted rates, or when the rates are considered separately for white and nonwhite.

To obtain a rank order of States in childhood mortality from rheumatic heart diseases and to make State-to-State comparisons more easily possible, the three age groups, the sexes, and the two race groups are combined in a single rate for each State (crude death rate). The results for the States confirm, with a few exceptions that in general the death rates are lower in the South than in the Northeast, especially than in the Middle Atlantic States; lower in the Pacific than in the Mountain States. This geographic tendency in the individual States becomes much more distinct if the rates for the white and nonwhite children are separately ranked, thus taking account of the greatly varying race composition of the individual states. 39 references. 3 appendixes. 22 tables. 2 figures.

(*This 63 page bulletin on Childhood Mortality from Rheumatic Fever and Heart Diseases may be purchased from the Superintendent of Documents, Government Printing Office, Washington, 25, D. C., for 25 cents a copy.*—ED.)



(Average annual death rates per 100,000 in each specified group)

* FIGURE 1.—Death Rates for Acute Rheumatic Fever plus Diseases of the Heart in White and Nonwhite Children, by Age and Sex: United States, 1939-41.

* *Courtesy U. S. Children's Bureau, Federal Security Agency*

The First Ten Years of Rheumatic Infection in Childhood. *Rachel Ash, Children's Hospital and the Medical School of the University of Pennsylvania, Philadelphia, Pa.* Am. Heart J. 36.89-97, July 1948.

Results are reported of a study of 588 children with rheumatic fever, with discussion limited to the first ten years following the initial illness. Of the children, 266 were boys; 323, girls; 110, Negro; 478, white. The average age at onset was 6.9 years, ranging from 17 months to 12 years. Seven were less than 2 years of age at time of onset; nineteen, less than 3 years. At the ten-year period, 91.3 per cent (537 children) had been located.

The mortality was highest among the forty-four children with acute primary carditis at onset, 30.2 per cent of whom ran a rapidly fatal course and 58 per cent of whom were dead at ten years. Regression of cardiac signs occurred in only one child. Of 47 children with insidious carditis at onset, 38.3 per cent were dead at ten years. Regression of cardiac signs occurred in four cases. Of 47 children with myalgia and vague joint pains at onset, 38 per cent already had signs of rheumatic heart disease when first seen; 10 per cent were dead in ten years. Of 107 children with chorea as the original manifestation, clinical signs of valvular heart disease were present in 22 (20.5 per cent) after recovery from the initial illness. At ten years, thirteen (13.7 per cent) were dead of heart disease. Regression of cardiac signs had occurred in two cases; progression in twenty-two. Of 343 children with acute arthritis at onset, signs of valvular heart disease were present after recovery from the initial attack in 209 (61.1 per cent). Thirty-one (9.1 per cent) had died of rheumatic infection during the first year; eighty-seven (25.4 per cent) were dead at ten years. Regression of cardiac signs had occurred in twenty-one; progression in twenty-three. Chorea as a subsequent manifestation was noted in forty-six. Forty per cent of the entire group exhibited recurrences of rheumatic infection within the first two years; 58 per cent within five years; and 63 per cent within ten years. Thus, of the 537 children, 318 (59.2 per cent) had signs of organic heart disease after recovery from the initial illness and thirty (9.4 per cent) subsequently lost these signs.

There were 131 deaths (24.4 per cent) due to rheumatic infection, twelve to bacterial endocarditis, and eight to unknown or unrelated causes. The average age at death for all these was 9.3 years, with limits ranging from 18 months to 18 years. Of deaths due to rheumatic infection, 47 (35.9 per cent) occurred within the first year and ninety-seven (74.0 per cent) within the first five years. Thus in childhood the first attack is by no means benign. More children die within the first year than in any succeeding year. The increment of deaths was greatest among those who developed recognizable rheumatic valvular damage in the initial attack. Relatively few deaths occurred among those who presented no clinical signs of cardiac damage after recovery from the initial attack. Chorea at onset is relatively benign because it is less likely to be associated with carditis than is polyarthritis or other types of rheumatic infection. Ten years after onset, 60.3 per cent of the rheumatic individuals were leading a normal existence with little or no limitation of

activity, the majority being those who had had no clinical evidence of heart disease at the termination of the initial attack. Death had occurred in only 5 per cent of the group in whom an original diagnosis of potential heart disease had been made, in comparison with a death rate of 42 per cent among those diagnosed as having rheumatic heart disease at onset. 2 references. 4 tables. 1 chart.

Longevity in Rheumatic Fever. Based on the Experience of 1,042 Children Observed Over a Period of Thirty Years. *May G. Wilson and Rose Lubschez, New York Hospital and Cornell University Medical College, New York, N. Y.* J. A. M. A. 138:794-98, Nov. 13, 1948.

This is an analysis of the clinical records of 1,042 children with rheumatic fever who were under observation over a thirty year period. The mean age at onset of the disease was 6.5 years. Among 226 deaths, 75.7 per cent were due to rheumatic disease of the heart and 10.2 per cent to subacute bacterial endocarditis was 2.2 per cent.

The clinical course of the disease was characterized by active carditis alone in 7 per cent, by one or more attacks of chorea in 25 per cent, by polyarthritis with or without chorea in 58 per cent and by joint pains in 10 per cent. Active carditis was clinically recognizable in only 45 per cent.

Cardiac involvement was demonstrable in every patient at last observation. Multiple valvular lesions and moderate or decided enlargement of the heart were observed in about 50 per cent. Auricular fibrillation occurred in 4 per cent of the patients. The auscultatory signs of valvular lesions regressed in one third of the group. One hundred and sixty-seven men served in the armed forces, and 162 women experienced a total of 288 pregnancies. There was no significant sex difference in the age-specific mortality rates. The highest mortality rate occurred within one year of onset. The highest death rates occurred between the ages of 1 and 4 years (33.2 per thousand) and 10 to 14 years (16.3 per thousand).

"An affected child has 4 out of 5 chances to survive childhood (to the age of 10 years), 3 chances out of 4 to survive puberty and 19 chances out of 20 to survive early adult life. The over-all chance to survive to the age of 40 years is 1 out of 2." 8 references. 2 figures. 2 tables.

Studies of Rheumatic Fever. Observations on Tonsillar Carriers of Hemolytic Streptococci. The Effect of Tonsillectomy and the Administration of Penicillin on Rheumatic and Nonrheumatic Fever Patients. *Harold G. Nelson and the Personnel of the U. S. Naval Medical Research Unit Four.* J. Infect. Dis. 83:138-46, Sept.-Oct. 1948.

The number and distribution of group A hemolytic streptococci were studied in the excised tonsils of 75 rheumatic fever patients (22 active and 53 convalescent) and 64 nonrheumatic fever patients. Nose-blow and throat cultures were taken on all patients three days prior to tonsillectomy. Throat

cultures were again performed on the day of tonsillectomy. Group A hemolytic streptococci were isolated from 2.7 per cent of the routine throat cultures and from 33.3 per cent of the excised tonsils of the rheumatic fever patients. No significant difference was found in the percentage of group A streptococci recovered from the tonsils of patients with continuing activity as compared with those in the inactive phase of rheumatic fever. The incidence of group A streptococci recovered from the throat and excised tonsil cultures of the nonrheumatic fever patients was 3.1 per cent and 15.6 per cent, respectively. 12 references. 3 tables. 2 figures.—*C. Whitlock, Jr.*

Cerebrospinal Fluid Sugar During Tuberculosis Meningitis and its Relation to the Reducing Power of Streptomycin (*La glicorachia in corso della meningite tubercolare e suoi rapporti con il potere riducente della streptomicina*). *Alvaro Masi and Nicola Menabuoni, Florence, Italy.* Riv. Clin. Pediat. 46:372-80, June 1948.

The level of spinal fluid sugar is generally low during bacterial meningitis and a rise has been regarded as a sign of diminished bacterial activity. In 80 patients with tuberculous meningitis treated with intrathecal streptomycin, cerebrospinal fluid sugar levels rose rapidly following earliest treatment, from levels of 10 to 20 mg. per cent to as high as 60 to 100 mg. per cent, without relationship to unchanged clinical signs. In vitro studies of various lots and brands of streptomycin, including purified salts, revealed a significant reducing capacity of the drug itself which is relatively more marked in dilute solution. In 0.1 cc of solution, 4 units of streptomycin revealed a reducing capacity equivalent to 0.163 to 0.243 mg. of glucose. Certain aldehyde groups present on the streptomycin molecule are responsible for such reactions. During suspension of intrathecal therapy levels promptly fell to lower values. An evaluation of bacterial activity on the basis of spinal fluid glucose levels is therefore unreliable during intrathecal streptomycin therapy.

It was coincidentally discovered that diffusion of intrathecal medication from the lumber to the suboccipital fluid is markedly reduced by elevated protein concentrations in the fluid. 4 references. 5 figures. 6 tables.—*A. M. Bongiovanni.*

(*In terms of milligrams of glucose per 100 cc. of fluid, the above figures are significant. This reducing capacity of streptomycin is not generally known. Diffusion of medication in spinal fluid is also important. Little has as yet been published on this topic.*—ED.)

Streptomycin Treatment of Tuberculosis Meningitis. *Streptomycin in Tuberculosis Trials Committee of Medical Research Council, Dr. Geoffrey Marshall, Chairman.* Lancet 1: 582-96, Apr. 17, 1948.

This report analyses the results in 105 cases of tuberculosis meningitis (children and adults) treated with streptomycin after a minimum of 105 days observation of survivors.

The dosage schedule employed was 20 mg. per pound of body weight per day intramuscularly (daily dose not to exceed 2 Gm.) given in divided 6 or 12 hourly portions. Intramuscular streptomycin treatment was given for at least 3 months. In addition 50 to 100 mg. daily was given intrathecally for varying periods of time to some of the patients. Despite the fact that CSF levels of 3-16 Gm. of streptomycin per cc. could be achieved from intramuscular streptomycin alone, the results in the group receiving intrathecal streptomycin in addition were significantly better than those with intramuscular streptomycin alone. Of the 28 patients receiving intramuscular treatment alone 78 per cent died; of the 72 patients receiving intrathecal streptomycin as well, 58 per cent died. The two groups of patients were comparable in all other respects. The clinical impression obtained was that prolonged courses of intrathecal streptomycin (i.e., more than 3 to 6 weeks) eventually cease to be beneficial and become harmful and that periods of complete rest from streptomycin therapy were also beneficial.

It was found that while patients were on intramuscular streptomycin alone, the cerebrospinal fluid streptomycin level was a valuable prognostic index. When the meningitis was advancing the level would rise and vice versa. A rising streptomycin cerebrospinal fluid level was therefore considered an indication for another course of intrathecal streptomycin. The cerebrospinal fluid sugar level was found to be the next best prognostic index.

During intrathecal streptomycin therapy peak levels in the cerebrospinal fluid ranged between 750 and 2000 Gm. per cc. The necessity for prolonged followup care and study in a sanatorium is emphasized including repeated examination of the spinal fluid.—*C. Whitlock, Jr.*

15. Liver, Kidneys, Spleen

Use of Continuous Caudal Analgesia for Control of Hypertension in Acute Nephritis. *James G. Hughes, George S. Lovejoy, Harvey D. Lynn and Robert A. Hingson, Memphis, Tenn.* Am. J. Dis. Child. 75:291-308, March 1948.

The authors emphasize the dangers of extreme hypertension in children with acute nephritis. Hypertension may be a contributing factor in the onset of cardiac decompensation, and the angiospasm believed to cause the hypertension may cause cerebral anoxia with associated nervous system manifestations. Hypertension occurring with the late toxemia of pregnancy may be markedly reduced by the use of continuous caudal analgesia. This method was tried for 6 patients having acute nephritis with hypertension which did not respond to the usual measures, including magnesium sulfate.

The first patient was a 10 year old girl with acute nephritis complicated by severe hypertension and cardiac decompensation. In spite of magnesium sulfate and other measures, the blood pressure rose rapidly, and pulmonary edema developed. When the child was considered almost moribund, con-

tinuous caudal analgesia was established, using 1.5 per cent metycaine hydrochloride. The blood pressure fell precipitously from 200/180 to 140/100 in ten minutes after the injection, and to 130/100 in 30 minutes. Cardiac compensation was swiftly reestablished, the child awakened from coma, conversed quietly with her physicians, and dropped off to a restful sleep. Uneventful recovery occurred. A 6 year old child with acute nephritis and cardiac failure also responded well to caudal analgesia with a reduction of blood pressure, and recovered. In the other 4 patients caudal analgesia produced prompt, often repeated reduction in blood pressure, but the improvement was temporary. Oliguria was affected very little or not at all.

The authors suggest that caudal analgesia reduces hypertension by paralyzing the sympathetic nerve fibers to the blood vessels in the portion of the body involved in the regional anesthesia. This would result in dilatation of the blood vessels to the lower extremities with pooling of blood, probable dilatation of the splanchnic bed, and probable increased blood flow to the kidney which may combat a possible renal ischemia.

The technic is the same as for obstetric patients. A 16 guage caudal analgesia needle was used for these children. The anesthetic agent was 1.5 per cent metycaine hydrochloride. Suggestions for test doses and maintenance doses are given. The obstetric literature dealing with the use of caudal analgesia to reduce hypertension is reviewed.

Since the time-tested methods of treating acute nephritis usually work well, caudal analgesia should be reserved for selected cases which do not respond satisfactorily to these methods, particularly the use of magnesium sulfate. Until the limitations and hazards of the method as applied to children are more fully known, the procedure is recommended for trial in the following types of nephritic patients: (1) patients whose hypertension is rising to extreme levels in spite of properly directed therapy with magnesium sulfate and other measures; (2) patients who have acute nephritis with cardiac failure and hypertension, especially those with pulmonary edema; and (3) nephritis patients with severe hypertensive encephalopathy. 5 references. 2 figures.

(*In some cases, usually those with large urinary volume, magnesium sulfate fails to reduce the blood pressure. This newer method of reducing the hypertension would have a real place in therapy in such cases. The fall in blood pressure without a corresponding diuresis is similar to the effect of magnesium sulfate.*—ED.)

16. Metabolic and Systemic Disorders

Acrodynia. *Hsi-Chi Chao and Fu-Tang Chu, National Peking University Medical College, Peiping, China.* Chinese M. J. 66:371-76, July 1948.

Although reported frequently from Europe, America and Australia, acrodynia is distinctly rare in China where all kinds of deficiency diseases are

common. During his 20 years at the Hospital of Peking Union Medical College, Fu-Tang Chu has seen only 2 cases. Both are reported in detail, with a review of the literature.

Both cases presented the classical syndrome of acrodynia: hyperirritability, anorexia, insomnia, tachycardia, excessive sweating, erythematous rash on the trunk and typical raw beef hands and feet with intense itching, and blood pressures of 128/90 and 145/100 mm. Hg. respectively. Both recovered completely after illnesses of more than 16 months. Thiamine chloride 20 mg. twice a day, nicotinic acid 100 mg. three times daily, yeast 3 Gm. daily and liver extract 4 cc. once a day, were used in the infant of 19 months without any convincing effects.

In view of the rarity of acrodynia in contrast with the frequency of various deficiency diseases in China, in addition to the absence of response to the hypervitamin therapy, nutritional factors as the primary etiologic cause of the disease can most likely be ruled out. 28 references.—*C. L. Kao.*

(*The negative relation between acrodynia and malnutrition adduced by this report is an argument for some other mechanism of pathogenesis — mercury poisoning, for example, which is the latest hypothesis.*—ED.)

17. Milk; Infant and Child Feeding

Clinical Treatment of Hypogalactia by Hormonal Methods. *Margaret Robinson, St. Thomas's Hospital and University College Hospital, London, England.* Brit. Med. Bull. 5:164-66, 1947.

In evaluating the effects of hormonal treatments on lactation, a group of 82 puerperal women were used as controls. These were given no treatment, or treated with massage, a proprietary galactagogue, inactive pills or daily intramuscular injections of physiological saline. Their mean output of milk at one month was 5.9 ounces per day before treatment started. It rose to 8.0 ounces per day during treatment. At one month it had risen to 8.4 ounces per day, and then began to fall. At six months the mean output had fallen to 3.5 ounces per day.

Dried thyroid gland in doses of 30 milligrams two to four times a day failed to stimulate lactation in all classes of women, whether begun after the end of puerperium or on the 6th or 7th day. On the other hand, daily doses from 0.25 to 0.6 Gm., begun soon after delivery, proved stimulating, so that about 50 per cent of the women with hypogalactia were producing 16 ounces of milk per day before discharge from hospital. Similar results were secured with 1.6 mg. of thyroxine per day from 3 to 5 days. No signs of thyrotoxicosis were encountered. Crude anterior pituitary extract, injected intramuscularly once daily for 5 consecutive days, evoked no increase in lactation.

Attempts to stimulate the growth of nipples with estrogens have resulted in complete failure. The most extreme cases of inverted nipples, however, became everted after inunctions of 5 per cent stilbestrol in peanut oil into the base of the nipples 4 to 6 times daily during the last 4 weeks of pregnancy. Weaker preparations and control inunctions of peanut oil had no effect.

Some women were given 5 milligrams of hexestrol by mouth every 4 hours for 1 to 3 weeks before delivery. When the subsequent labor was normal, the onset of lactation was not delayed, and the secretion of milk was often copious. When operative interference was needed, or with long and difficult labor, the onset of lactation was often delayed and the secretion scanty or absent.

The too-rapid onset of lactation which causes engorgement of the breasts at the 2nd or 3rd day of the puerperium was found controllable by estrogens. A 5 milligram tablet of hexestrol or stilbestrol was taken as soon as the patient felt a sensation of tightness in her breasts. Additional tablets were taken after each nursing period until the risk of engorgement was past. From 3 to 18 tablets were necessary. This treatment did not suppress lactation, but kept the milk flowing freely, and prevented failure in those women who had the ability to lactate normally. The infant was not removed from the breast during this treatment. Lumpy breasts in the puerperium were cured by 5 milligrams tablets of stilbestrol or hexestrol, or 1 milligram tablets of dienestrol, until the lumps were gone. The infant was kept on the breast during the treatment. The output of milk increased in those women with the ability to produce milk was absent. Five per cent stilbestrol in peanut oil rubbed into the crack, healed cracked nipples in a few days.

Lactorrhea was most common in the first weeks of lactation, being most common among the "sprinter" class of milkers. It can be cured from the 4th week of lactation by giving the mother 5 milligrams of hexestrol or stilbestrol by mouth after every nursing over a period of 5 to 7 days. It cannot be controlled during the puerperium. Most cases spontaneously recover in the 3rd week of lactation. When lactorrhea and failing lactation are present together in the later weeks, treatment with estrogens increases the milk yield and seems to prevent subsequent failure.

Threatened breast-abscesses of the deep glandular type occur from the 2nd week of lactation onward. The mother usually belongs to the "sprinter" class of milker. Hexestrol (5 milligrams every 4 hours) cured the condition, provided treatment was commenced before the pressure inside the lobules had destroyed the cells. The infant was not removed from the breast during treatment. As many as 7 attacks have been noted in the same woman during the six months of her lactation. "Patients who belong to the sprinter class of milkers should be discouraged from expressing their milk after feeding the infant, as this leads to early failure. Instead, they should be provided with a box of 5 milligram tablets of hexestrol, and be told to take one pill after each breast-feed, if they feel that their breasts have not been emptied by the infant. In this way breast-abscesses of the deep glandular type can be prevented." So long as the infant is kept at the breast, estrogens do not seem to suppress lactation. One week's course of estrogens can also reduce the force with which the breast sprays the milk into the infant's mouth.

Women classified as "stickers" and "non-starters" seem to be deficient in thyroid secretion, and therefore need intensive thyroid therapy in the puerperium in order to start lactation. Treatment after the 12th day of the puer-

perium has been useless. "Sprinters" and abscess-producers need estrogens intermittently throughout the whole six months of lactation, in order to prevent breast abscesses and early failure of lactation.

Infantile mastitis can be cured by local application of estrogens to the infant's breasts, 5 per cent stilbestrol in 5 per cent peanut oil. The ointment is applied under a cotton bandage for 24 to 48 hours. Then gentle pressure causes the milk to spray out and the mastitis disappears. The fluid expressed has been proved to be milk. 10 references.

Incidence, Causes, and Prevention of Failure of Breast-Feeding. *Harold Waller, British Hospital for Mothers and Babies, London, England.* Brit. Med. Bull. 5:181-85, No. 2-3, 1947.

It is estimated that at present not more than half the babies born in Britain are breast fed for longer than 3 months, and that by 6 months the proportion has fallen to 40 per cent. The process of breast involution begins with distension of the alveoli by residual milk and is followed by disintegration of the secreting cells. If production is to be maintained, tension within the breast must be kept below the point at which the rate of secretion is reduced. With women who produce excess milk, therefore, it is important to remove the excess by manual manipulation after the baby has been fed. The danger of high milk tension is specially great in the early days, when the milk "comes in," and it may be possible to induce any outflow. Unless the engorgement is quickly overcome, regression sets in. A large proportion of women who seem to have little milk give this account of the start of lactation.

Proper emptying of the breast is also important. In many women, unfortunately, one or both nipples fail to reach the complete stage of development which makes it possible for the infant to draw the nipple far back into its mouth. For retracted nipples, women are given a pair of glass shields which they wear during pregnancy under a well-fitting brassiere. The shield has a central opening which is placed over the nipple; the brassiere exerts enough pressure to force the nipple through the opening and loosen its attachment to the breast. They are also taught the technic of removing the milk by hand. Of 300 primiparas treated in this manner, 79 per cent were successfully breast feeding at 6 months.

The procedures must be supplemented by a constant watch on milk tension during the puerperal period. Synthetic estrogens are given to check the very sudden outburst of secretion that overtakes some women. The dosage has to be judged by each woman's reaction. As soon as a crack is found in the nipple, nursing is witheld until it is securely healed, the milk meanwhile being expressed by hand.

It is important, also, to feed the infant at intervals spaced according to his needs and the frequency of the "draught" reflex in the mother. The "let-down" or "draught" represents a reflex essential to proper nursing. This coincides with the outrush of milk which follows within a second or two after the baby draws the nipple into its mouth, and may occur spontaneously. The

baby's intake is found by test-weighing, and the number of nursings required in the day is calculated to bring the amount up to its caloric needs. A long interval at night is a disadvantage if it leads to the breasts becoming overfull and the baby crying with hunger. The length of time a baby spends at the breast is continued as long as he can be persuaded to drink. Overfeeding is not encountered. Most babies profit by getting the milk quickly. With feeding directed in this way, some two-thirds of the mothers have a definite appreciation of the "draught" reflex before they leave the hospital. This same method works successfully with young prematures. The mother is taught how to remove the milk by hand and sends or brings it once daily to the ward. 9 references.

(*The observations summarized in the two foregoing abstracts represent the best available information on how to stimulate lactation during the puerperium and how to keep the milk flow going once it is started. The mechanisms which govern human lactation are still far from clear.*—ED.)

The Incidence of Breast Feeding in Hospitals in the United States. *Katherine Bain, U. S. Children's Bureau, Federal Security Agency, Washington, D. C.* Pediatrics, 2:313-20, September 1948.

The data presented, obtained in the American Academy of Pediatrics Study of Child Health Services, are the first national figures on the incidence of breast feeding in maternity wards in the United States.

A one-week record of the type of feeding of all infants discharged alive (under 8 days, and 8 days of age and over) from the newborn nursery was supplied by 72 per cent of the 3,500 hospitals of 25 or more beds which admitted women for delivery. The sample was representative of hospitals in all regions and in rural and urban areas, and of hospitals of all sizes.

Type of feeding at time of discharge was reported for 39,171 infants. At the time of discharge approximately one-third were on the bottle only, and two-thirds were on breast only or breast and bottle. The proportion of breast feeding at time of discharge was greater in areas away from metropolitan centers. The proportion of bottle feeding was greater in middle-sized (100-249 beds) hospitals than in large or small ones.

There were wide regional differences in the incidence of breast feeding. In the Northeast region 61 per cent of the infants were discharged on artificial feeding as compared with 18 per cent in the South and Southwest. The States in which the proportion of infants entirely artificially fed exceeded 50 per cent were all in the northeast area. The states with the highest incidence of bottle feeding were Connecticut and New Hampshire with 70 and 72 per cent respectively. The states with the lowest incidence of bottle feeding were South Carolina and Alabama with 10 and 11 per cent, respectively.

The group of infants discharged from the hospital under 8 days of age had a higher incidence of breast feeding than those who remained 8 days or longer. 10 references. 1 figure. 4 tables.

Cup Feeding of Newborn Infants. *Robert C. Fredeen, University of Kansas School of Medicine, Kansas City, Mo.* Pediatrics 2:544-48, November 1948.

For 10 years the author has been practicing the feeding of infants from a cup or glass, starting in the newborn period. This method of feeding is stated to assure the artificially fed baby the same pleasurable physical contact with the mother as is enjoyed by the breast fed infant, since during feedings the infant is cradled in his mother's left arm similar to the manner used by the mother who feeds her child from the breast. The procedure varies depending upon the baby, but usually the whole feeding is given in 5 to 10 minutes. The method has been employed with full term infants, premature and immature babies, infants with harelip and cleft palate and older infants both healthy and sick. Those with a harelip or cleft palate are said to take their food rapidly and without apparent difficulty. With practice, spillage usually becomes negligible after the first few feedings. Regurgitation, vomiting and colic are minimal. The impression has been gained that cup feeding instituted at birth did not lead to psychologic difficulties either in infancy or later childhood. 2 references. 1 figure. 2 tables.

(*The wisdom of early cup feeding as here recommended must be seriously questioned, although the author's observations suggest that the psychologic needs of the infant for the motions of sucking are perhaps being currently overemphasized by some authors. Before sponsoring a widespread change-over from customary habits of breast and bottle feeding one would like to see the advocates of this method bring forward objective proof that cup fed babies are free from mental difficulties, and remain so throughout later life, in view of the growing body of evidence from the psychiatric field that sucking while nursing satisfies certain deepseated needs of the personality. There ought also to be controlled statistical studies on the comparative incidence of aspiration pneumonia in large groups of infants fed with the cup as compared to bottle and breast.*—ED.)

The Effect of Early Oral Feeding Versus Early Oral Starvation on the Course of Infantile Diarrhea. *A. W. Chung and B. Viscorova. New York University, New York, and University Children's Clinic, Bratislava, Czechoslovakia.* J. Pediat. 33:14-22, July, 1948.

Data are presented on 115 patients with infantile diarrhea treated alternately by early oral starvation (55 cases) and full caloric feeding (60 cases). Correction of shock, dehydration, and acidosis received immediate attention in all cases.

In the starved group, water alone was given by mouth in the first 24 hours. Following this a formula made from powdered milk, sugar, and water was given at the rate of 20 calories per kilogram of body weight on the first day and increased at the rate of 20 calories per kilogram each day or less depending on the course of the diarrhea.

Those receiving the full feeding regime received the same type of formula equivalent to 80 calories per kilogram per day for babies over 6 months of age and 100 to 120 calories for those under 6 months. This was begun as soon as possible after reparative parenteral therapy and temporarily discontinued only if vomiting occurred or if the infant refused the feedings.

The average duration of diarrhea in the fed group was 6.1 days and in the starved, 7.8 days. A more prompt and persistent weight gain was observed in the fed group despite the larger volume of stool excreted.

The series was too small to draw conclusions as to mortality although 7 deaths occurred in the fed and 5 in the starved group, a total mortality of 10.4 per cent. 3 references. 3 charts. 2 tables.—*R. N. Paul.*

Terminal Heating of Infant Formula. I. Bacteriological Investigation of Low-Pressure Technique. *F. R. Smith, R. D. Finley, H. J. Wright, and E. A. Louder. Pet Milk Research Laboratories, Greensville, Illinois.* J. Am. Dietet. A. 24:755-59, September 1948.

Bacteriologic tests on formulas prepared by aseptic procedures at several hospitals have shown that the majority of the formulas contained some micro-organisms. The terminal heating method of preparation would seem to offer safety from accidental contamination. This is a report of bacteriologic studies on the low-pressure technique of terminal sterilization.

A low-pressure water vapor terminal heating procedure which maintained infant milk mixtures at 100 C. (212 F.) for 15 minutes produced the following results: (a) Sterilization of a regular evaporated milk formula and of nipple surfaces in the case of all samples tested; (b) Complete destruction of Escherichia coli, Staphylococcus citreus, and Streptococcus pyogenes when formulas were inoculated with substantial numbers of these test organisms; (c) Another test organism, Bacillus globigii, a non-pathogenic heat-resistant, spore-forming aerobic bacillus, was completely destroyed in the majority of samples, and in the remainder was reduced to counts below 10 organisms per milliliter.

This terminal heating method has been found to be satisfactory for both evaporated and whole milk. No significant physical changes in the milks were observed. Nipple hoods furnished substantial protection from air-borne organisms, but should not be relied upon for complete protection from a heavy aerosol. The advantages of a nipple hood of prefabricated transparent rubber film were demonstrated. 4 references. 2 tables. 2 figures. 2 plates.

Terminal Heating of Infant Formula. II. Bacteriological Investigation of High-Pressure Technique. *F. R. Smith, R. D. Finley and E. A. Louder, Pet Milk Research Laboratories, Greenville, Ill.* J. Am. Dietet. A. 24:760-63, September 1948.

Sterility tests on infants feeding milk mixtures autoclaved at 230 F. for 10 minutes have shown this treatment adequate for terminal heating. No significant physical injury to the milk seemed to be sustained as the result of this processing.

18. Miscellaneous

The Development of the Hypospray for Parenteral Therapy by Jet Injection. *Robert A. Hingson, Johns Hopkins Hospital, Baltimore, Md.* Anesthesiol. 10:66-75, January 1949.

Nipple covers, when used during autoclaving of assembled formula units, provided appreciable protection of nipple surfaces against air-borne contamination during subsequent storage. Of the nipple hoods tested, those of prefabricated transparent rubber film proved best.

Improper cleaning of bottles permitted contamination with heat-resistant organisms which survived autoclaving at 230 F. for 10 minutes. 1 reference. 4 tables. 1 figure.

(*One practical point when employing this method is to apply the nipple covers loosely rather than tightly, or see that they contain small perforations. Otherwise they may blow off during the heating.*—ED.)

The hypospray in its latest form of development is a compact instrument the size of a two-battery flashlight. It is so constructed that 125 pounds of spring pressure can project a plunger, 0.5 cm. in diameter, into a bullet-size container of 0.25 cc. volume called a metapule. In the blunt nose of the bullet is a microscopic orifice 0.003 inch (approximately 76 microns) in diameter. The force of 125 pounds builds up a pressure of approximately 3900 pounds per square inch, which ejects a column of liquid from the metapule at a velocity of 600 miles per hour. Frank H. J. Figge, Professor of Experimental Anatomy at the University of Maryland, has determined that this will force the material through the skin, into the subcutaneous tissue and along fascia planes, and even into the muscle planes on the volar surfaces.

Some of the difficulties with this method of injection (Hingson and Hughes, 1947) have been the cost of the instrument and the metapules; the present limited maximal dose of 0.25 cc.; the need for differently lined containers for different active drugs; the possible injury to tissue from the jet injections; the relatively wider dispersion of injected material as compared with the needle-syringe method which might prove a disadvantage in the injection of toxoids when slow absorption is desired; the mechanical difficulties associated with maintaining operation of this more technically complicated apparatus. It has been shown (R. V. Brown) that jet discharges should not be made in the neighborhood of large blood vessels unless the drug to be injected is safe both in concentration and is pharmacologically safe for intravenous administration. The probability of unintentionally

penetrating a major vein is small but the risk is always present. Upon general release of the instrument, patients needing self-medication should be instructed as to safe sites for injection.

From experiences with jet injection in more than 5,000 patients, the author believes that the likelihood of inadvertent intravenous injection is less than with the needle and syringe method. Furthermore, since the diameter of the jet is only 1/37 that of a 26-gauge needle, there should be less trauma with the hypospray than with needle and syringe. Other advantages of hypospray injection over that of the needle and syringe technic are: complete absence of pain in half the subjects so injected, and diminution in pain in the majority of the remainder; sterilization of the instrument before use is unnecessary; children about to be injected do not fear the instrument. ("Their actual experience with one injection convinces them that subsequent injections will be painless or nearly so"); when many injections are to be given, this instrument eliminating multiple sterilizations of equipment. For the administration of drugs by daily injection over long periods, such as insulin and penicillin, this is recommended as the instrument of choice. The method holds great promise in the field of therapeutic nerve block for relief of pain. 4 references. 7 figures.

Susceptibility of Mongoloids to Infection. II. Antibody Response to Tetanus Toxoid and Typhoid Vaccine. *Morris Siegel, The Public Health Research Institute of The City of New York, New York.* Am. J. Hyg. 48:63-73, July 1948.

A companion paper on the frequency of pneumonia and dysentery due to Sh. dysenteriae (Sonne) described a consistently higher incidence in mongoloids than nonmongoloids. (Am. J. Hyg. 48:53-62, July 1948.) The results were related to quantitative differences in the degree of susceptibility exhibited by the individuals examined. In seeking an explanation, a long-term study was conducted on antibody formation following parenteral antigenic stimulation.

The concentration of circulating antibodies following inoculation of tetanus toxoid and typhoid vaccine was observed in 20 mongoloid and 20 nonmongoloid individuals over a period of 3 years. On the whole, the antibodies response was less marked and of shorter duration in the mongoloid group than in the nonmongoloid. The percentage of poor reactors to a given antigen was greater in the mongoloid group than the nonmongoloid. These differences in quantitative response may represent a defect in defense mechanism which might be related to host susceptibility and hormonal deficiencies characteristic of the mongoloid. 23 references. 6 tables. 1 figure.

Condition of Children in Western Germany. *A. P. Meiklejohn, University of Edinburgh, Ed., Scotland.* Lancet 2:619-35, Oct. 16, 1948.

This paper, based on observations made during two recent visits to Germany, describes the state of health of the child population of Western Germany and the sources of its food. The relevant vital statistics are sum-

marized. The general level of health and nutrition among the great majority of children in bombed cities is relatively satisfactory, but a minority of about 10 per cent, comprising the "vulnerable groups", are in poor physical condition. The overwhelming impression gained by this visit to Germany is the dangerous social and psychologic environment in which the children of the bombed cities are growing up. In comparison with this, their nutritional health is much less important. 2 references.

Hyaluronidase in Fluid Administration. *J. Schwartzman, A. T. Henderson, and W. E. King, New York Medical College, New York.* J. Pediat., 33:267-73, September 1948.

Hyaluronidase has been shown to increase the rate of fluid absorption 12 times. This suggested unlimited possibilities of fluid administration in infants without the arduous task of searching for suitable veins for intravenous administration.

Six individuals (4 children and 2 adults) were studied before and after administration of 0.02 mg. per individual. As far as could be determined there were no harmful effects.

Various dilutions of the drug were tested with regard to optimal concentration for fluid administration and skin testing. It was found that the greater the dilution the greater the time required for absorption. For skin testing, 0.01 mg. of hyaluronidase was found best. Of 108 skin tests only 9.3 per cent showed positive reaction.

The drug was used in conjunction with adrenalin, penicillin, procaine and streptomycin and in each case absorption was greatly facilitated.

The degree of pain associated with clysis was about the same whether or not the drug was given but pain disappeared more rapidly when hyaluronidase was used. It was found possible to give continuous clysis for at least 5 days by using the drug. 23 references. 5 tables.—*R. N. Paul.*

Severe Erythema Multiforme of the Pluriorificial Type (Stevens-Johnson Syndrome) Resulting in Blindness in a Patient Treated with Trimethadione (Tridione). *Bertram Shaffer and Paul Morris, Mt. Sinai Hospital, Philadelphia, Pa.* Pediatrics 2:30-34, July 1948.

A case of severe erythema multiforme bullosum of the orificial type is described, resulting in complete blindness due to bilateral involvement of the cornea. The eruption occurred in a white boy, aged 6½ years. Both trimethadione (Tridione) and Polyansin (anterior pituitary extract) had been administered for "general retardation of mental development".

Widespread involvement of the skin with bullous and purpuric lesions occurred. This was associated with bullous and erosive lesions in the orificial mucosae including the conjunctivae, nares, nasal chambers, lips, mouth, tongue, pharynx and glans penis. The child was acutely ill with fever,

leukocytosis, and wheezing chest rales. After a week, the skin lesions began to subside but the severe eruption on the musosae continued for a period of several more weeks. At the end of the second week, the left cornea became the site of a bleb which ruptured and became an abscess. The right eye behaved similarly, and the lens herniated through a corneal perforation. Complete blindness resulted. Penicillin was given parenterally throughout the acute period.

Passive transfer tests with the drugs being taken were negative, but it was felt that Trimethadione was probably the cause of the eruption. 19 references. 1 figure.

(*Erythema multiforme is a "reaction pattern" which can be induced by a wide variety of infections, vaccines or drugs. All range of severity occur from barely visible lesions of the skin and mucous membranes to those associated with the death of the patient. Whenever the diagnosis is considered a careful search for a specific etiologic agent is mandatory.*

The Stevens-Johnson Syndrome is also not an etiologic entity. Sometimes a specific agent appears to be associated with the onset of symptoms as in the case described above. In most instances, however, no cause can be found. Many of the patients have been thought to be suffering from a specific infection, particularly of viral origin, but no such agent has ever been isolated. The association of skin lesions with lesions of the mucous membranes and genitalia suggests that the syndrome belongs with the ill-defined group of illnesses classified under the term erythema multiforme and perhaps should have been so named in the article.—ED.)

19. Musculoskeletal System

Value of Routine Roentgenograms of the Wrist in a Pediatric Service *M. G. Peterman, W. B. Frey, and J. D. Kaster, Milwaukee, Wisconsin.* Am. J. Dis. Child. 75:671-87, May 1948.

Routine roentgenograms of the wrist were studied on 333 infants and children admitted to a hospital pediatric service and on 351 private patients in a pediatrician's office in an attempt to evaluate their usefulness in the detection of suspected or unsuspected pathology. In both series, 10 per cent of the total number of roentgenograms revealed abnormal findings. 19 references. 5 figures. 6 tables—*M. Maresh.*

(*Although clues to diagnosis may be obtained from routine roentgenograms of the wrist, there would seem to be oversimplification of the separation of the normal from the abnormal in this study. Certainly the use of the basal metabolism test should not be overlooked in the diagnosis of hypothyroidism. It may be added that determination of "bone age" seldom reveals disorders which should not have been suspected on the grounds of history and general physical features.*—ED.)

Treatment of Genu Valgum. The Discarded Iron. *H. A. Brittain, Norfolk and Norwich Hospital,* Brit. M. J. 2:385-7, Aug. 21, 1948.

The knock-knee iron or brace is not only an appliance of doubtful efficacy, but it causes unfortunate psychologic effects in growing children by making them feel inferior to other children. Rickets is given in prominent texts as the most common cause of knock-knee, others being tuberculosis, poliomyelitis, fractures, and "loose knees". Actually, the commonest causes are laxity of ligaments (loose-knees), quadriceps insufficiency, and overweight. Estimate of the extent of genu valgum is made not only from the intermalleolar distance, which will vary with size of the child, but by the angle between femur and tibia. Treatment consists of wedging the shoes, 3/16 in. on the inner side of both sole and heel, in all cases. All except the mildest cases are also treated with night splints, the best of which is Lloyd's night splint. This consists of two pieces locked together. One keeps the knee in extension; the other provides lateral pressure. They are held on by bandage. Only rarely is an operation necessary. 7 references. 3 figures. 1 table.—*F. Hertzmark.*

Fracture of the Anterior Spine of the Ilium. Report of Four Cases and Discussion of Treatment. *J. Roswell Gallagher, Andover, Mass.* Pediatrics 2:186-89, August 1948.

Four case reports of fracture of the anterior spine of the ilium emphasize the symptoms which characterize this injury and the efficacy of brief conservative treatment. This fracture should be suspected when sudden severe pain develops in the inguinal region during the course of some strenuous exertion or athletic activity; its occurrence during short foot races has led to the name "Sprinter's Fracture". The initial pain is severe, and there may be vomiting; raising of the extended leg is impossible and there is tenderness over the injured area. When these signs and symptoms are present a roentgenogram should be taken to distinguish fracture of an anterior iliac spine from such disturbances as tear of the quadriceps muscle. Some of these injuries can be prevented if athletes are compelled to "warm-up" prior to making those maximal efforts which put severe strain on the points of origin of the large muscles of the thigh. In none of these cases was surgical intervention found necessary. In each instance complete recovery followed two to three weeks of bed rest with the knee flexed, after which activity was gradually increased. Nailing the fragment, applying a plaster spica, or six weeks bed rest did not improve the results. 5 references.—*Author's abstract.*

Legg-Perthes' Disease: A Syndrome of Many Etiologies? With Clinical and Roentgenographic Findings in a Case of Gaucher's Disease. *S. Z. Draznin and Karl Singer. Michael Reese Hospital, Chicago, Illinois.* Am. J. Roentgenol. 60:490-97, October 1948.

Since Legg-Perthes' disease is frequently found with a variety of disorders, that diagnosis should initiate a search for the underlying pathogenic factors. A case is presented with typical Gaucher's disease which had been diagnosed at the age of five. During the next 18 years the patient developed numerous skeletal changes, among them Legg-Perthes' disease. Review of the literature revealed several other instances of the simultaneous occurrence of Gaucher's disease and Legg-Perthes' syndrome and the suggestion is made that Gaucher's disease be added to the list of possible causative mechanisms of Legg-Perthes' disease. 44 references. 5 figures. 1 table.—*M. Maresh.*

20. Nervous System

Sturge-Kalischer-Weber Syndrome of Bilateral Distribution. *C. Worster-Drought.* Brit. M. J. 2:414-16, Aug. 28, 1948.

This is presented as the first report of bilateral intracranial calcifications in a child with Sturge-Kalischer-Weber syndrome. A four and one-half year old child had extensive cutaneous naevi on both sides of her face, scalp, trunk and extremities, more marked on the left; right hemiparesis; generalized convulsive seizures predominant on the right; and mental deficiency. The convulsions started at four months. Roentgenograms of the skull at 19 months revealed fine, extensive calcification over both cerebral hemispheres, most marked on the left. The cerebral lesion is believed to be a capillary angioma of the leptomeninges. The involved cerebral hemisphere may be smaller than the opposite cerebrum. 13 references. 4 figures.—*B. J. Shuman.*

Calcified Intracranial Tuberculomas. *H. Stephen Weens, Atlanta, Ga.* J. Pediat. 33:328-335, September 1948.

One proved and 2 presumptive cases of calcified intracranial tuberculomas are presented. In two children the lesions were multiple; in one, solitary. On roentgenographic examination calcified tuberculomas of the brain have a characteristic serrated and angular appearance. They may occur in any portion of the brain and rarely measure more than 3 cm. in diameter. 17 references. 6 figures.

21. Newborn Period, Prematurity

Septicemia of the Newborn. *R. M. Todd, University of Liverpool, England.* Arch. Dis. Childhood 23:102-06, July 1948.

Of 15 cases of neonatal septicemia, Staphylococcus aureus was the offender in 11 cases, Staphylococcus albus in 2, Streptococcus hemolyticus in 1 and Bacillus coli in 1. Antemortem blood cultures were positive in 11 cases.

Systemic symptoms were anorexia, weight loss, diarrhea, hemorrhage, jaundice, vomiting and rarely a palpable liver and spleen. Localizing symptoms depended on the portal of entry. The umbilicus appeared normal while in the other 4 it appeared inflamed. In 3 the respiratory tract appeared to be the portal of entry, though none had localized respiratory tract signs. In 4 cases, 1 of septic arthritis, 2 of osteomyelitis of the maxilla and 1 of septicemia, the portal of entry was not apparent.

The author points out that the onset of septicemia in the newborn may be insidious, since the newborn frequently shows no hyperpyrexia, rigors or convulsive seizures. The mortality rate in this series was 60 per cent in spite of penicillin and sulfonamide therapy.

When a newborn infant loses weight or fails to gain weight or shows vague symptoms of anorexia and diarrhea, septicemia should be suspected and blood cultures should be taken immediately. Treatment should be started before results of blood culture are known. Only in this way can one hope to reduce the mortality. 30 references. 1 table.—*A. N. Evans.*

Anaerobic Metabolism in the Newborn Infant. I. On the Resistance of the Fetus and Newborn to Oxygen Lack. *James L. Wilson, Helen S. Reardon and Makio Murayama, with the assistance of Bruce Graham, M. U. Tsao, and M. L. Baumann, Ann Arbor, Michigan.* Pediatrics, 1:581-92, May 1948.

A short review is given of various studies which lead to the conclusion that premature and full term newborn infants, as well as newborn of lower animals, have a partially anaerobic metabolism in fetal life which is lost soon after birth. The following is advanced in support of this statement: 1) A report by other workers on the resistance of newborn animals to oxygen lack. 2) Studies by other workers and the authors on acid-base balance which show that normal newborn infants have a true acidosis as measured by low pH and low plasma carbon dioxide content of the blood and an elevated excretion of organic acids in the urine. 3) The authors' observations that the irregular anoxic type of breathing of premature infants in atmosphere is changed to a regular type of respiration with the administration of 70 per cent oxygen, indicating an initial under-pulmonary ventilation. This exists in spite of the fact that both arterial and venous blood studies show a true acidosis which should be associated with over-pulmonary ventilation.

The authors suggest that the low carbon dioxide content in blood is not due to excessive loss in the lungs, but is rather the result of incomplete combustion of intermediary metabolites giving increased organic acids and decreased carbon dioxide and water. If organic acids (other than carbon dioxide) are end-products of carbohydrate metabolism, this would explain the apparent paradox of a low blood carbon dioxide content as actually found coexisting with a diminished alveolar ventilation assumed from evidence of oxygen lack.

All this is of considerable interest as it bears upon fetal physiology. Furthermore: 1) A low carbon dioxide content and pH (true acidosis) may be

normal and usual in premature babies and, except when excessive, need not be combatted by attempts to give alkaline solutions by mouth or vein. 2) Oxygen therapy may be beneficial even in healthy premature infants. 3) Previous studies of metabolism in premature infants may be inaccurate due to failure to allow for a partially anaerobic metabolism. 17 references. 5 figures. 6 tables.—*Author's abstract.*

The Physiological Basis for Resuscitation of the Newborn. *David M. Little, Jr. and Ralph M. Tovell, Hartford Hospital, Hartford, Conn.* Surg. Gyn. & Obst. 86:417-28, May 1948.

Fetal and neonatal mortality rates are improving but little, and since certain resuscitative procedures widespread in practice are based on extremely precarious physiological thinking, it is appropriate to review the subject of asphyxia neonatorum and its proper treatment.

Initiation of Respiration in the Newborn. There is clinical and experimental evidence to indicate that respiratory movements are not necessarily initiated at or after birth, but may begin in utero. Many authorities believe that such intrauterine respiratory movements occur only in the presence of fetal asphyxia. Others believe that the fetus is not normally apneic in utero, but that post-natal breathing is merely a continuation of intrauterine respiratory activity. Other theories have been propounded to explain the mechanism of the onset of fetal respiratory activity and the initiation of the first inspiratory gasp of the newborn. Mechanical trauma, insufficient oxygen, excess of carbon dioxide, and a change in the pH of the fetal blood have all been hypothecated as the necessary stimulus.

Asphyxia Neonatorum. Asphyxia neonatorum is a generic term used to describe lack of oxygen of varying severity occurring in the newborn infant, and may be classified in terms of physical findings into "the stage of depression", "the stage of spasticity", and "the stage of flaccidity". The etiologic factors include the age, parity, and health of the mother, the viability of the germ plasm, the immaturity of the infant, the presentation and position of the fetus, the medical induction of labor, the duration and type of labor, the complications of labor, the type of delivery, the analgesic and anesthetic agents and methods employed. Chemically, the syndrome is characterized by a decrease in the content of oxygen in the fetal blood, a secondary increase in the tension of carbon dioxide, an increase in the content of lactic acid, and a decrease in the pH of the fetal blood. The primary lesions of asphyxia neonatorum is atelectasis of the lungs; secondary lesions result from the anoxia of various tissues and organs, particularly the brain, liver, lungs and gastrointestinal tract. It has been demonstrated, both clinically and ex-

perimentally in animals, that permanent irreparable damage to the central nervous system, with corresponding personality and mental deviations, may result from anoxia of asphyxia neonatorum.

Methods of Resuscitation. The first requisite in the resuscitation of the asphyxiated newborn is the establishment of an adequate airway by gentle suction in the nares, mouth, pharynx, and, if necessary, the trachea. Trendelenburg position of 15, or at the most 30, degrees will aid in the drainage of secretions. An endotracheal catheter should be passed into the trachea not only for aspiration, but also, if necessary, to ensure maintenance of the airway. External stimulation, if used at all, should be extremely gentle, and only to promote the discharge of afferent impulses to the respiratory center from the skin, subcutaneous tissues and joints. Oxygen must be administered as soon as the airway is established and cleared. Carbon dioxide should not be used, since it is depressant to the anoxic respiratory center. Artificial respiration may be necessary to force oxygen down to the atelectatic lungs and various forms may be employed, including manual artificial respiration, Eve's rocking method, respirators of the Drinker type, mouth-to-mouth insufflation, inhalators such as the Kreiselman resuscitator, or resuscitators that provide an alternate increase and decrease of the pressure in the alveolar spaces such as the Ericson and Johnson resuscitator. It is an enigma that such artificial respiration if exerted with sufficient force to overcome the resistance to expansion of the atelectatic lungs, is capable of producing gross pulmonary damage. The warmth of the infant's body should be maintained throughout the resuscitative period and thereafter. Stimulatory drugs such as epinephrine, alpha-lobeline, pituitrin, camphor, coramine, picrotoxin, metrazol, caffeine and strychnine, by increasing the metabolism and therefore the oxygen demand of the already-anoxic brain of the newborn, are capable of doing more harm than good, and should not be employed. 256 references.—*Author's abstract.*

The Relation Between Infant Birth-Weight and Subsequent Development of Maternal Diabetes Mellitus. *J. P. Kriss and P. H. Futcher, St. Louis, Mo.* J. Clin. Endocr. 8:380-89, May 1948.

A study was made of the birth weights of infants born to 100 women destined later to develop diabetes mellitus and of infants born to two control groups of non-diabetic women. The findings led to the conclusions that (a) the birth of an infant weighing over 10 pounds may herald the development of diabetes in the mother; (b) the average birth weight of infants born to prediabetic mothers is greater than that of infants born to normal mothers; (c) women developing diabetes after the childbearing period are, to a large extent, mothers who have given birth to babies weighing over 10 pounds; (d) abnormally large babies are born to prediabetic women

more frequently than to normal controls; (e) the period between the birth of the first abnormally large infant and the development of clinical diabetes in the mother averaged about 24 years in this series, with a range of from 1 to 46 years.

On the basis of the data, a table has been constructed permitting rough estimation of the accuracy with which one may predict the subsequent development of diabetes in a woman giving birth to a baby weighing more than 10 pounds. As the birth weight of the baby rises, the prediction accuracy increases progressively and is greater than 60 per cent when the baby weighs more than 13 pounds. 13 references. 2 tables. 2 figures.—*Author's abstract.*

Studies in Prematurity. Part 4. Development and Progress of the Prematurely Born Child in the Pre-School Period. *C. M. Drillien, University of Edinburgh.* Arch. Dis. Childhood 23:69-83, June 1948.

Progress during infancy and early childhood was studied for all surviving infants entering the hospital during the years 1943-45. A random 1 in 10 sample of fullterm infants was used as control.

A significant difference was found between the ages at which premature and mature infants sat, stood, walked, and talked. The smaller the infant, the more marked was the retardation. Among mature infants there was little variation with increase of birth weight. No marked difference was found between the liability of premature and mature children to contract the specific fevers of childhood. Prematurely-born children showed a significantly higher incidence of nasopharyngeal and respiratory infection, this being especially marked in the first year of life.

Twenty-three per cent of the premature, and 15 per cent of the full-term children were reported as having behavior problems. Feeding problems were the most common especially among the premature group. These, as well as behavior disorders in general, were positively associated with poor health. No significant difference was found in the incidence of dental caries, nasopharyngeal infection, cervical adenitis, and rickets.

At any given age, average weight was found to rise steadily with increasing birth weight. The same trend was observed for height, though the differences were not so striking. The suggestion is made that the differences found after the first few years of life between prematurely born and fullterm children, as regards height, weight, and general development, are due largely to environmental factors, being the same adverse conditions as originally acted on the mother to produce the premature delivery. 22 references. 17 tables. 10 figures.—*A. N. Evans.*

22. Nutrition

Tuberculin Hypoergy and Anergy in Relation to the Nutritional State During the War Years. (*Ipoergia ed anergia tubercolinica in rapporto allo stato di nutrizione negli anni di guerra*). *G. Nichele and T. Clavelli, University of Rome, Rome Italy.* Pediatria internazionale 1:199-208, Jan.-March 1948.

The loss of tuberculin sensitivity in those previously positive has been known to follow acute infectious disease, exposure to cold and malnutrition. A study of 675 children with tuberculosis during the period 1936-44, revealed an actual increase in the incidence of the disease with a diminution in percentage of positive tuberculin reactors. In 1940, 87.5 per cent of patients were positive to dilutions of 1/5000-1/10,000 and in 1944 only 60.04 per cent were positive to dilutions ranging from 1/1000 to 1/100. The remainder were negative or doubtful. The diminution in response was most marked in the age group 7-10 years. The percentage of patients of suboptimal body weight in the same two periods was 30 and 50 respectively. The loss of immunologic mechanisms secondary to diets poor in proteins, fats and vitamins throughout the war is proposed as the responsible factors in this phenomenon. 23 references. 2 tables—*A. M. Bongiovanni.*

Disturbances of Carotene Metabolism in Childhood (*Perturbaciones del metabolismo de las carotinas en el nino*). *Augustin Castellanos, Havana, Cuba.* Rev.cubana.pediat. 20:377-91, July 1948.

The intestinal absorption of carotene depends upon the presence of bile salts, pancreatic secretions, and adequate adrenal function. In the blood, carotene exists in combination with serine and lipids. In the new born infant the carotene blood level has been reported as 27 gammas per cent.; at 18 months, 100 gammas.

In plant life, carotene is an important catalyst in carbohydrate metabolism. The sole value in man is as pro-vitamin A. In the human fetus, the source of vitamin A is maternal carotene. Vitamin A itself does not pass the placental barrier. The transformation of carotene into vitamin A occurs in the liver under the influence of an enzyme, carotenase, and is accelerated by thyroxin.

Carotenemia with blood levels exceeding 200 gammas is attributed to excess carotene ingestion or failure of transformation to Vitamin A. Since excess ingestion will not always produce high blood levels in all children, the latter cause is emphasized. Failure of hepatic function or hypothyroidism

as causes are cited in each of two patients aged 8 and 9 years respectively. The disturbances of carotene metabolism in diseases such as diabetes are not well understood.

Carotinosis cutis depends upon deposition of large quantities of carotene in the adipose tissue of areas with marked epithelial keratinization (palmar-plantar). Unknown metabolic factors other than carotinemia may enter into its casusation.

Acarotinosis most often results from failure of absorption as in pancreatic cystic fibrosis and congenital biliary atresia. Whether this condition is of clinical significance remains unknown. In 23 patients aged 6 to 21 months ill with toxemia accompanying chronic respiratory infections, the carotene blood levels were extremely low and in many instances zero. In one case treated by an intravenous colloidal carotene preparation with elevation of the blood level, there was improvement. 15 references. 1 figure. 1 table.—*A. M. Bongiovanni.*

(*The low levels of carotene reported in connection with respiratory infection were also accompanied by low Vitamin A levels. This has been a known occurrence in pneumonia and rheumatic fever. It may be that an increased demand for Vitamin A results in exhaustion of body carotene. Murrill, J. Clin. Invest.* 20:395, 1941, *showed that the Vitamin A reserves are maintained at the expense of endogenous carotene.*—ED.)

Recommended Dietary Allowances. Revised 1948.

Food and Nutrition Board, National Research Council. National Research Council Reprint and Circular Series No. 129, October 1948, Washington, D. C.

The accompanying table lists levels of nutrient intakes which the Food and Nutrition Board recommends as desirable. These recommendations represent levels high enough to cover substantially all individual variations in the requirements of normal people. The explanatory comments discuss a number of topics of interest in pediatrics.

With most of the nutrients, once the diet furnishes enough to meet functional need, further amounts supplied by the food are normally a matter very nearly of indifference. With a few nutrients, however, especially ascorbic acid, vitamin A and calcium, there is evidence from long-term (animal) experimentation that in the course of a lifetime one may derive increased benefit from levels considerably above those of ordinarily accepted adequacy. With calories, on the other hand, any considerable surplus tends to induce overweight.

The caloric allowances for children over one year of age have not been changed in this revision. At all ages caloric allowance should be related to size and activity. The greatest variation occurs in adolescence. A large active boy of 15 years may need as much as 5000 calories.

The protein allowances were derived from a compilation of balance studies of children of all ages. The intakes of protein per kilogram with which appropriate positive balances are obtained are 4 to 3.5 Gm. in infancy, 3 to 2.5 Gm. in early childhood, and 2 to 1.5 Gm. in late childhood and adolescence; the adult maintenance standard is 1 Gm. The amounts required depend on the size of the child and the quality of the protein. Infants fed human milk may thrive with a much lower intake than the recommended allowances.

The requirement for phosphorus cannot be considered alone but must be related to the intake of calcium and protein. Utilization of phosphorus, like that of calcium, varies with the amount of vitamin D.

The recommended allowances for ascorbic acid are derived from a conservative appraisal of all the evidence that is available; they will not produce "saturation" levels. More generous intakes will yield considerably higher concentrations in the tissues.

From 300 to 400 units daily of vitamin D commonly permits maximal retention of calcium in infancy when the calcium intake is satisfactory. Maximal calcium retention is associated with excellent skeletal growth and early dentition. Larger amounts of vitamin D do not increase calcium retention or the rates of growth or dentition.

There is no evidence to support the general opinion that prematurely born babies require more vitamin D than do babies born at term. Rickets in the premature is more often due to deficient intake of calcium and phosphorus than to a greater need for vitamin D. Because of the poorer utilzation of fat in prematurity a water-miscible preparation of vitamin D may be advisable.

RECOMMENDED DAILY DIETARY ALLOWANCES[1] (*Condensed Table*)

REVISED 1948

Food and Nutrition Board, National Research Council

	Calories[2]	Protein, gm.	Calcium, gm.	Iron, mg.	Vitamin A,[3] I.U.	Thiamine,[4] mg.	Riboflavin,[4] mg.	Niacin (Nicotinic acid),[4] mg.	Ascorbic acid, mg.	Vitamin D, I.U.
Children up to 12 yrs.[5]										
Under 1 yr.[6]	110/2.2. lb. (1 kg.)	3.5/2.2 lb. (1 kg.)	1.0	6	1500	0.4	0.6	4	30	400
1-3 yrs. (27 lb., 12 kg.)	1200	40	1.0	7	2000	0.6	0.9	6	35	400
4-6 yrs. (42 lb., 19 kg.)	1600	50	1.0	8	2500	0.8	1.2	8	50	400
7-9 yrs. (58 lb., 26 kg.)	2000	60	1.0	10	3500	1.0	1.5	10	60	400
10-12 yrs. (78 lb., 35 kg.)	2500	70	1.2	12	4500	1.2	1.8	12	75	400
Children over 12 yrs.[5]										
Girls, 13-15 yrs. (108 lb., 49 kg.)	2600	80	1.3	15	5000	1.3	2.0	13	80	400
16-20 yrs. (122 lb., 55 kg.)	2400	75	1.0	15	5000	1.2	1.8	12	80	400
Boys, 13-15 yrs. (108 lb., 49 kg.)	3200	85	1.4	15	5000	1.5	2.0	15	90	400
16-20 yrs. (141 lb., 64 kg.)	3800	100	1.4	15	6000	1.7	2.5	17	100	400

[1] The recommended allowances can be attained with a good variety of common foods which will also provide other minerals and vitamins for which requirements are less well known.

[2] Calorie allowances must be adjusted up or down to meet specific needs. The calorie values in the table are therefore not applicable to all individuals but rather represent group averages. The proper calorie allowance is that which over an extended period will maintain body weight or rate of growth at the level most conducive to well-being.

[3] The allowance depends on the relative amounts of vitamin A and carotene. The allowances of the table are based on the premise that approximately two-thirds of the vitamin A value of the average diet in this country is contributed by carotene and that carotene has half or less than half the value of vitamin A.

[4] The fact that figures are given for different calorie levels for thiamine and niacin does not imply that we can estimate the requirement of these factors within 500 calories, but they are added merely for simplicity of calculation. In the present revision, riboflavin allowances are based on body weight rather than caloric levels. Other members of the B complex also are required, though no values can be given.

Foods supplying adequate thiamine, riboflavin, and niacin will tend to supply sufficient of the remaining B vitamins.

[5] Allowances for children are based on the needs for the middle year in each group (as 2, 5, 8, etc.) and are for moderate activity and for average weight at the middle year of the age group.

[6] Needs for infants increase from month to month with size and activity. The amounts given are for approximately 6 to 8 months. The dietary requirements for some of the nutrients such as protein and calcium are less if derived largely from human milk.

For older infants and children the actual requirement has not been accurately determined. It is known, however, that 400 units daily is ample for good calcium retention in children when the milk intake is appropriate. A few children do not require a supplement of vitamin D for good calcium retention, but the majority do. In adolescence the need for vitamin D is as universal and as great as in infancy.

In view of the large number of babies with intracranial damage at birth and the possible relationship of these lesions to vitamin K deficiency, it is suggested that vitamin K be given to pregnant women during the last month of pregnancy. One milligram parenterally to the mother will meet the needs of the infant for several days. A daily oral dose of 1 mg. is ample. When the mother has been treated in this manner, the newborn infant needs no supplement of vitamin K during the short period preceding ingestion of food. The prothrombin level of the baby is higher in the first days after birth if vitamin K is given to the mother before delivery than if given to the baby at birth. A suitable dose for the newborn is 1 mg., and this will satisfy the need until food is taken. In fact, a single dose of 10 to 20 micrograms will cover the first five days, for the daily requirement of the infant is only about 1 microgram.

Milk is an outstanding source of calcium, riboflavin, and many other nutrients. Without milk or its products it is almost impossible to meet the daily calcium needs from ordinary foods. In 1947, 75 per cent of all the calcium, and nearly half of the riboflavin in our national food supply was furnished by milk and milk products. No other food group supplies more than 4 per cent of the calcium.

Citrus fruits and tomatoes are more important sources of vitamin C than the leafy green and yellow vegetables, whose high vitamin C content is impaired by cooking and storage. 122 references. 3 charts.

(The "Recommended Allowances" are more than the minimal requirements of average individuals—they represent intakes which are set sufficiently liberally to be "suitable for maintenance of good nutritional status". Enough evidence has been gained from long term animal experimentation and observations of individual variation of need to justify some leeway above the minimal needs. It is on this basis that the "Recommended Allowances" have been formulated. The scientific evidence is set out in considerable detail.

The original pamphlet repeatedly emphasizes that the amounts of each food substance recommended are intended as safe averages and do not necessarily apply to individuals. Recognition of the great variation in needs from one person to another is particularly important when dealing with growing children. Most often the pediatrician is dealing with family groups which include children and instruction must be given in terms of foods as eaten. To be especially stressed are the basically important groups of natural foods which must be represented in each day's diet. If the child is accustomed

to taking these basic groups from infancy, and if they are provided in sufficient variety, one seldom needs to think in terms of calories, grams or milligrams. In other words, quantities can be left to the child. Adjustments will sometimes be necessary in relation to economic status, illness, obesity, racial or other eating habits and perhaps other conditions, but the basic food groups must be included. Public and family education are needed in the preparation and cooking of food to maintain its full nutritive value.

The basic food groups which could be given are as follows: (1) milk, cheese; (2) meat, eggs, cheese, fish, fowl; (3) citrus fruits, tomatoes, raw cabbage; (4) colored and leafy vegetables, preferably partly raw; (5) fruits, partly raw; (6) whole-grain cereal foods; (7) vitamin D in some form is necessary in most regions except perhaps in the summer. Other carbohydrates and fatty foods supply further calories where needed.

The Recommended Daily Allowances are revised every year or so as knowledge of nutrition increases. Every pediatrician should keep abreast of the new editions.—ED.)

23. Parasitic Diseases

A Preliminary Report of the Successful Treatment of Amebiasis with Aureomycin. *L. V. McVay, R. L. Laird and D. H. Sprunt, University of Tennessee College of Medicine and The John Gaston Hospital, Memphis, Tenn.* Science 109:590-91, June 10, 1949.

Three adults ill with gastrointestinal infections caused by Endamoeba histolytica were treated with aureomycin in dosages of approximately 2 to 2.5 Gm. daily. Clinical recovery was almost immediate and the stools became negative within a few days. Laboratory tests showed that E. histolytica is readily killed by aureomycin. 3 references.

Giardia Lamblia. The Incidence and Results of Infestation of Children in Residential Nurseries. *E. H. Brown, London, England.* Arch. Dis. Childhood 23:119-128, June 1948.

A study of Giardia lamblia infestation was made in a nursery with accommodation for 30 mothers and 156 children up to 3 years of age. An initial survey yielded no positive stools in children less than 1 year of age. Subsequent examinations were limited to children between one and 3 years of age.

Of 139 admissions, 26.6 per cent were positive initially. In contradistinction, 80 per cent of the children who had been in the nursery for longer than three months were positive. By the end of 2 months of hospitalization 61.1 per cent of the new admissions had become positive. Examination of the adults in the nursery showed only 3.1 per cent positive stools. Two other comparable nurseries were surveyed at the same time and the infestation rate was 46 per cent for one and 61 per cent for the other.

The character of the stools of those children positive on admission was not different from those negative on admission but it was thought that the stools became more greyish, loose and greasy with prolonged hospitalization. Tests for fecal fat on the two groups failed to show any difference. Infestation had no effect on the hemoglobin and did not seem to be related to intercurrent diarrhea. The height and weight of the children who were infested was subnormal in general and this subnormality increased with duration of hospitalization.

Five days of therapy with Mepacrine [quinacrine, atabrine] (0.075 Gm. daily for children less than 18 months of age and 0.1 Gm. daily for children over 18 months of age) produced a gradual and significant increase in the height and weight of these children. The stools returned to normal and the health improved in general. 9 references. 14 tables.—*A. N. Evans.*

(It is often stated that giardia infestation is asymptomatic and not provocative of constitutional disturbances. In the nursery outbreaks described here, however, the increases in height and weight after treatment are highly significant and argue for the clinical importance of this infestation. Celiac syndrome has also been seen in giardiasis to improve with treatment. Maris, (Penna. M. J. Apr. 1942) *found infestation to be associated with otherwise unexplained abdominal pain which was relieved following treatment with atabrine and the clearing of infestation. Many children with recurrent upper abdominal pains and poor appetites owe their symptoms to giardial duodenitis. Maris found that atabrine in doses of* 45 *mg.* (¾ *grain*) *for smaller children and* 90 *mg.* (1¼ *grain*) *for the larger children cleared up the infestations if given twice a day for only three days.*

One must remember in this connection, that stool examinations will often be negative in children who by duodenal drainage can be shown to be heavily infested.—ED.)

24. Pathology, Anatomy, Bacteriology

See Contents for Related Articles

25. Physiology, Biochemistry

Effect of Galactose on the Utilization of Fat. *Curt P. Richter, The Physichobiological Laboratory, Johns Hopkins Medical School, Baltimore, Md.* Science, 2808:423-454, Oct. 22, 1948.

Evidence is presented to suggest that galactose plays an important part in the utilization of fat. Three series of Norway rats were used. One series of rats had access only to galactose; a second, only to oleo; a third, to both oleo and galactose (in separate containers). A control series had no

food at all. The 15 rats with no food survived from 3 to 6 days, with an average of 4.3 days. Thirteen rats on galactose alone survived from 4 to 8 days, with an average of 6.2 days. The 10 rats on oleo survived from 19 to 38 days, with an average of 32.4 days. The 13 rats on oleo and galactose survived from 47 to 92 days, with an average of 69.3 days; this was over twice as long as on oleo alone, and over 11 times as long as on galactose alone.

Comparison of the amounts of oleo and galactose eaten by the rats when they had simultaneous access to these two foodstuffs showed that the galactose contributed an average of only 15.3 per cent of the total. For some of the rats the average daily galactose intake fell below 5 per cent of the total. The calories received from galactose could not have contributed substantially to the length of time that the rats survived.

The rats with access to galactose ate more oleo than did those having access only to oleo, and much less galactose than those with access only to galactose. In further experiments the ingestion of a mixture of oleo and galactose (9 or 10 parts of oleo to 1 part of galactose) similarly prolonged the survival time. In contrast a mixture of oleo and glucose in equal proportions or as 1 part oleo to 9 parts of galactose failed to increase the survival times above those of rats on oleo alone.

All these results indicate that galactose may have a specific effect on the utilization of fat. "Should the results of further experiments on rats disclose that galactose in such small amounts has the same effect on other fats as it does on oleo, and that galactose has a superior action to all other sugars in this respect, fortification of common fats and oils with small amounts of lactose, galactose, or skim milk powder might be considered for the diet of man". 11 references.

(*Milk has long been regarded by pediatricians and nutrition scientists as the most nearly perfect single natural food. This study on the possible importance of galactose in the utilization of fat may be just one more indication of the importance of milk in nutrition. The intestinal enzyme lactase acts on the lactose of milk to produce glucose and galactose.*

The use by SCIENCE of "oleo" rather than "oleomargarine" gives a stamp of approval to the convenience and efficiency represented by the shorter term.—ED).

Modification of Fat Absorption in the Digestive Tract by the Use of an Emulsifying Agent. *Chester M. Jones, Perry J. Culver, Gladys D. Drummey and Anna E. Ryan, Boston, Mass.* Ann. Int. Med., 29:1-10, July 1948.

Experiments are described to determine whether addition of the emulsifying agent "PSM" (polyoxyethylene sorbitan monooleate, known also as "Tween 80") would improve the uptake of fat from the bowel in diseases affecting the function of the small intestine. It was found that when PSM was added to meals in 1.5 Gm. quantities for patients having assorted difficulties in fat absorption, significant reductions occurred in the amounts

of fecal fat. Vitamin A tolerance curves were taken under standard conditions in a group of 16 normal subjects. Specimens were taken while fasting and at intervals of 3, 5, and 7 hours after the ingestion of 200,000 units of vitamin A ester in fish liver oil. Two weeks after control studies a set of the tests were repeated, with 2.0 Gms of PSM added to the capsules containing the fatty solution of Vitamin A. The peak level of vitamin A obtained in the serum was essentially the same in the composite control curves and following the use of an emulsifying agent, but absorption was accelerated after the use of PSM inasmuch as the peak of absorption occurred at about three hours as compared to a peak at five hours in the control studies. In patients suffering from such conditions as subtotal gastrectomy, sprue, pancreatic fibrosis and regional enteritis, the addition of PSM to a fatty solution of vitamin A resulted in important increases in fat absorption.

It is suggested that agents such as polyoxyethylene sorbitan monooleate facilitate fat absorption because of their ability to lower surface tension. Being nontoxic, they may be of benefit in chronic digestive disturbances with impaired ingestion of fat. 7 references. 3 tables. 3 figures.

(*In view of the results here reported, the emulsifying agent PSM may well prove a valuable addition to our armamentaria in the treatment of a number of clinical conditions associated with poor absorption of fat. Further clinical reports may be anticipated.*—ED.)

26. *Psychology, Psychiatry*

Childhood Behavior Sequelae of Asphyxia in Infancy. With Special Reference to Pertussis and Asphyxia Neonatorum. *George B. Rosenfeld and Charles Bradley, Emma Pendleton Bradley Home, E. Providence, R. I.* Pediatrics 2:74-84, July 1948.

A study was made of the character of the behavior of 154 children with maladjustment. Of these 126 had pertussis during the first three years of life; 28 had had difficult resuscitation at birth and a diagnosis of asphyxia neonatorum seemed justified. A control group was studied of 100 other children with behavior disorders, who had not experienced asphyxiant illness, or convulsive disorder or related conditions such as head injury or poisoning which might be suspected of having damaged the central nervous system. Studied also were 126 children who had had pertussis after the third year of age.

It is concluded that a fairly uniform overt behavior pattern becomes apparent in maladjusted children who have experienced asphyxiant illness in infancy. Six cardinal behavior characteristics make up this syndrome: 1. Unpredictable variability in mood; 2. Hypermotility; 3. Impulsiveness; 4. Short attention span; 5. Fluctuant ability to recall material previously learned; and 6. Conspicuous difficulty with arithmetic in school. Although each of these six characteristics may occur by itself or in other associations in almost any psychiatric disorder, the combination of all or most of these

traits in one individual seemed to be related to an early history of asphyxia. Seventy children in the pertussis group (55.6 per cent), 17 children (60.5 per cent) in the asphyxia neonatorum, and only 7 in the control group (7 per cent) exhibited five or more of these symptoms. The importance of asphyxia from pertussis tends to drop off after the period of infancy and above age four the figures tend to approximate what is obtained in the control children. Conclusions can not be drawn from these data as to the frequency of this syndrome in all children who have suffered from these types of asphyxia in infancy. When a child comes to clinical attention with most "of the cardinal traits which his history indicates are presumably related to antecedent asphyxiant illness, the clinician may be reasonably sure that he is dealing with behavior somewhat conditioned by a disordered function of the central nervous system. Treatment for the child and guidance for his parents and teachers may then be planned accordingly."

Because of the life-long character disturbances which can follow asphyxia in infancy, prophylaxis becomes extremely important. Cautions are given with respect to early immunization for infectious asphyxiant diseases, conscientious management of delivery particularly in regard to sedative or anesthetic drugs which may retard fetal respiration, and the giving of adequate oxygen to infants suffering from disorders associated with anoxemia.

The Psychopathology of Comic Books. A Symposium. *Frederick Wertham, Chairman. Articles by G. Legman, H. L. Mosse, P. Elkisch, and M. L. Blumberg.* Am. J. Psychotherapy 2:472-90, July 1948.

In this symposium, the "con" side of the intensifying controversy over mass-produced "comic" books is unanimously defended. An attempt to qualify, by individual case studies and group questionnaire methods, the effects of the estimated five hundred million comic books now deluging yearly the children in the United States has led the individual authors to recognize certain recurrent Art-motifs in the comic literature itself as well as fairly clear-cut reaction patterns of the avid juvenile readers.

Examining the comic books themselves, these investigators find the stereotyped themes to include: (1) the glorification of crime, in spite of half-hearted, censor-enforced retractions of this theme; (2) the weighted emphasis on the right of the individual to administer his own two-fisted version of the existing law; (3) the constant association of cruelty with sexuality; (4) the wide-spread implication that "good" conquers "evil" only by violence. The conscious reaction of children to these repetitive motifs appear to fall into positive and negative categories which are, perhaps surprisingly, almost evenly mixed, as Elkisch's questionnaire to grade-school and college students of both sexes and mingled races show. The doubt which these children show about their immediate need for more and bigger comic books appears to be in accord, these authors feel, with the less consciously evident but characteristic reactions of children (wtih some age differences) to "comic" material. Because of their vivid mental imagery, children tend (1) to confound fantasy with reality (younger children

especially), and (2) to place themselves in the positions of the vividly depicted characters on both sides of the moral fence "at the same time". This divided identification illustrates the mingled feelings of attraction and repulsion which children harbor toward violence, anger, and other aggressive displays, as a result of their constantly conflicting inner urges toward conformity and rebellion in relation to parental and societal restrictions.

The participants in this symposium concede that children go through stages of emotional development in which their feelings reproduce, to some extent, the violent "comic" battles, and that fantastic adventures, often of a violent nature, can afford a constructive outlet for the anger and tensions arising from immediate frustrations which are inevitable, particularly during the progress of the pre-school and later the adolescent child toward socialization and maturity. Nevertheless, the authors unitedly feel that the child's ultimate adjustment to the demands of an adult civilization is not furthered by an overbalanced all too-commercialized emphasis by comic books on "primitive" and generally negative feelings which repeatedly stimulate aggressive fantasies without the constructive resolution or clear separation from reality which the age-old fairy tales appear to offer. Healthier outlets are needed for the turbulent aggressive feelings exhibited by so many children in these frustrating disturbed years.—*D. G. Prugh.*

(*One further consideration might be added to the above indictment of "comic" books. Children of a generation ago read lurid tales of violence and adventure but in this way they learned to love to read. Once having come to enjoy reading, the quality of their chosen subject-matter almost always improved, and they were led by easy stages to better and better literature. Good books broaden one's interests, furnish enrichment to life, and teach one to view mankind with some perspective. Comic books, in contrast, form a dead end. Many children never grow beyond them.*

The same trend is seen with television. It is not uncommon today for a whole family to settle in front of the television screen in dull satiation, turning away only to read comic books and daily papers. Outdoor play and the city life become uninviting. There are often few books in such homes which could interest any of the family. Even when one member tires sufficiently of the television show to open a book, the radio's din makes reading impossible. The schools can and will use visual education to great advantage, but some means must be continued for leading children to the world's great literature.—ED).

27. Public Health, Epidemiology

Trends of Diarrheal Disease Mortality in the United States 1941 to 1946, Inclusive. *F. M. Hemphill, U. S. Public Health Service, Communicable Disease Center, Atlanta, Ga.* Pub. Health Rep. 63:1699-1711, Dec. 31, 1948.

For the period 1933 to 1946 inclusive, the trend of mortality from diarrheal causes has been downward, especially in children under two years of age. The decrements have been spasmodic rather than regular, with the most significant annual decrement during 1946.

The decrease in mortality during 1946 occurred primarily in the summer and fall months. Most of the children who died were from rural areas; the large majority were under 1 year of age. The factors which seemed most likely to have caused the decrease of 1946 were improved medical treatment and the widespread use of DDT to allay the prevalence of reactors. 15 references. 5 figures. 4 tables.

Diarrheal Disease Control Studies. I. The Effect of Fly Control in a High Morbidity Area. *James Watt and Dale R. Lindsay, Bethesda, Md. and Atlanta, Ga.* Pub. Health Rep. 63:1319-34, Oct. 8, 1948.

The development in recent years of more potent insecticides, particularly DDT, has made it possible to carry out a broad scale experiment designed to answer the following questions: (1) Can flies be controlled in urban populations by insecticidal methods under the limitations of civilian life? (2) What effect, if any, will such control have on the acute diarrheal diseases of the community, particularly those caused by specific infection with the Shigella and Salmonella groups of micro-organisms?

Hidalgo County, Texas, was selected for the study because it had a large amount of infectious diarrheal disease as well as a major fly problem. Also, towns in the County could be divided into two comparable areas, one to be treated and the other to be left untreated. The investigation included spraying the study area with DDT and making laboratory analyses of cultures taken from children under ten years of age, the group in which the infection rate is highest. A total of 1,300 cultures was taken each month on a voluntary basis, family histories were taken monthly from individuals participating in the study and an analysis was made of reported deaths resulting from diarrheal disease.

The treated towns were originally sprayed every six weeks and periodic counts were taken of the fly population in those areas. When material increase of flies was observed in the treated areas, spot re-treatments were given at intervals, some as often as twice weekly. As the fly control measures progressed, a marked decrease was noted in cases of diarrhea due to Shigella infections in the treated towns. When treated and untreated areas were reversed the incidence of cases soon became reversed, thus confirming the results. The effect on Shigella infections was greater than on infections with the Salmonella group of organisms. Thus fly control would have greater potential value as a health measure in those areas where Shigella infections predominate as a cause of acute diarrheal disease.

An evaluation is now being made to determine the best methods of achieving satisfactory community fly control, since the use of insecticides is only a temporary measure which must be repeated at frequent intervals. 3 references. 4 tables. 5 graphs.

Handkerchiefs in the Transfer of Respiratory Infection. *K. R. Dumbell, J. E. Lovelock and E. J. Lowbury.* Lancet. 2:183-85, July 31, 1948.

In a study of the transfer of respiratory infection an attempt was made to determine the number of potentially infective particles liberated by shaking of dry handkerchiefs. An average of 136,000 bacteria-carrying particles were shaken from normally used handkerchiefs. The particles were resistant to aerial disinfectants (ultraviolet, triethylene glycol, lactic acid and alpha-hydroxy-alpha-methyl-butyric acid). It is concluded that hankerchiefs are most important in contaminating the air with micro-organisms from the respiratory tract. 9 references. 3 tables. 2 figures.—*B. J. Shuman.*

(*The shaking of bed linen and blankets from an infected bed are other sources of air contamination.*—ED.)

28. Respiratory System

Recurring and Chronic Cough in Children. Role of Sinusitis. *E. E. Brown, Ashland, Ore.* Northwest Med. 47:435-38, June 1948.

From fourteen years' observation of children with recurrent and chronic cough, the conclusion is drawn that these coughs are often dependent on chronic sinusitis, which focus must be treated. The recurring cough is not limited to the northern states, for it is reported in Tennessee and in semi-tropical areas such as Los Angeles and Miami.

Almost invariably dependent on chronic sinusitis are recurring and chronic bronchitis, bacterial asthma and bronchiectasis. Enlargement of these nodes may be secondary to purulent sinusitis, as proved experimentally in dogs by Mullin and Ryder.

Indirectly related to sinusitis may be atopic asthma secondary to ingested foods and inhaled pollens and epidermals. Sinusitis permits allergic reactions, including cough, to occur during the winter and spring months. The same antigens may cause no reaction in warm weather when sinusitis is least active.

Unrelated to sinusitis are the chronic coughs which follow inhalation of a foreign body and those due to tuberculosis, atelectasis, mediastinal tumor and cardiac failure.—*Condensed author's abstract.*

(*Many expert otolaryngologists and bronchoscopists experienced in children's disorders feel that the relationship between chronic sinusitis and chronic bronchitis or bronchiectasis is the exact opposite of what here stated. The sinusitis, in their opinion, is the result rather than the cause of the bronchial infection. The persistent cough exhibited by the children continually exposes the upper nasal passages to recurrent showers of germ-laden mucus. The nasal sinuses even though drainage is free have no opportunity to attain a state of normal health.*—ED).

Bronchoscopic Observations on the Pulmonary Aspects of Fibrocystic Disease of the Pancreas. *Joseph P. Atkins, University of Pennsylvania, The University Hospital, and the Children's Hospital of Philadelphia, Philadelphia, Pa.* Ann. Otol. Rhin. and Laryng. 57:791-802, September 1948.

Bronchoscopic examination of children with fibrocystic disease of the pancreas presents fairly characteristic findings. On introduction of the bronchoscope the lumen becomes obscured by the presence of extremely viscid, purulent or, occasionally, blood-stained mucus. When this is aspirated the hyperemic bronchus shows marked expiratory intrusion of the posterior bronchial wall into the lumen, producing a bronchus whose cross section is crescentic. In this respect the bronchus resembles that seen in the asthmatic patient. The common picture is that of a hyperemic, sometimes granular mucosa with thickening of the bronchial spurs. A few patients may present the picture of tracheobronchitis with the usual moderately thin mucopurulent secretion. There is a tendency for the pulmonary infection to subside and flare up. The marked reduction of pulmonary reserve is manifested in two ways: first by the frequency and severity of the cyanosis which occurs during bronchoscopy. The routine use of oxygen insufflation through the bronchoscope during examination greatly reduces the frequency of cyanosis but does not always prevent it. A second manifestation of decreased pulmonary reserve is that the children often become cyanotic during the paroxysms of pertussis-like cough which are such a prominent feature of the disease.

Bronchoscopic aspiration usually relieves the obstructive character of the respiration. The duration of the improvement is variable, sometimes being less than 24 hours. Repeated bronchoscopic aspiration may reduce the viscosity of the secretion. The bronchopulmonary drainage being thus improved, antibiotic and chemotherapeutic drugs are more effective.

Multiple organisms are usually present in the bronchial secretion. Staphylococcus aureus has been found almost always, though one patient showed Bacillus pyocyaneus in pure culture. Other organisms found have been Streptococcus viridans, pneumococcus, diphtheroids, Micrococcus catarrhalis, hemolytic streptococci, Escherichia coli and Haemophilus influenzae. Three typical case histories are given. 7 references. 5 figures.

29. Skin, Teeth, Hair

See Contents for Related Articles

30. Social, Economic, and Organizational Problems

See Contents for Related Articles

31. Surgery, Anesthesia

Acute Hematogenous Osteomyelitis. *Edward B. Self, Babies Hospital, New York, N. Y.* Pediatrics 1:617-26, May 1948.

A review and appraisal is made of 138 cases of hematogenous osteomyelitis seen between 1930 and 1946 with a comparison of the outcome before and after the advent of sulfanilamide and penicillin therapy. Infection elsewhere in the body, or trauma, seem to be the chief predisposing factors. There were 82 cases due to hemolytic Staph. aureus, in 40 (approximately 50 per cent) of which the blood culture was positive. There were 27 cases of infection due to hemolytic streptococcus of which 13 cases had positive blood cultures. Pneumococcus was responsible three times, salmonella twice, and gonococcus once. The femur, tibia, and humerus were most commonly affected in that order. In 24 or 17 per cent of the total cases, more than one bone was involved. Seventy per cent of the patients with streptococcal infections (19 out of 27) were under three years of age. Sixty per cent of those with staphylococcal infections (77 out of 111) were over three years of age. Of the streptococcal infections 5 cases were termed chronic and 22 acute, a ratio of approximately 1 to 4. Of the staphylococcal infections the numbers were 57 chronic and 74 acute, or a ratio of 1 to 2. Roentgen findings were positive in 111 cases, negative in 11, and uncertain in 16.

Of the cases treated by surgery only, 37 per cent healed completely without sequelae; in contrast, of an equal number treated by chemotherapy, only 71 per cent were healed. The mortality rate of the surgically treated group was 13 per cent; of those receiving chemotherapy, 2.6 per cent. There were many fewer deaths and the hospitalization period was shorter in the chemotherapy-treated group.

Massive doses of penicillin in the earliest stages of the disease constitutes the best treatment. Emphasis should be on the "treatment of the child", rather than treatment of the bone. Surgery should be postponed in the early stages and used later only to drain abscesses of the soft parts or abscesses of the bone which are well localized and not regressing. With chronic osteomyelitis, however, radical removal of the diseased bone and sinuses with primary closure of the wound is the treatment of choice. Immobilization, penicillin, and obliteration of dead spaces with muscle and skin grafts are important adjuncts to success. 1 reference. 7 figures. 4 tables.

Bilateral Nontraumatic Iliofemoral Thrombophlebitis in a Child. *H. L. Myers and N. Artsis, Oceanside, N. Y.* Am. Heart J. 36:295-98. August 1948.

A 6-year-old boy with bilateral nontraumatic iliofemoral thrombophlebitis is presented. The onset followed an ill-defined respiratory and gastrointestinal infection. The arterial pulsations disappeared first in the left and then in the right lower extremity as the thrombophlebitic process

spread. Therapy consisted of elevation of the foot of the bed on eight-inch blocks, warm fomentations, 30,000 units of penicillin every three hours, and paravertebral sympathetic nerve blocks. Bromsalizol was used in order to prolong the effect of the blocks and obviate the necessity for repeated blocking. Anticoagulants were not used. 5 references. 1 figure.

32. Tumors

Primary Teratomatous Chorionepitheliomas of the Ovary. Report of a Case. *H. M. Oliver, and E. O. Horne, Worcester City Hospital, Worcester, Mass.* New England J. Med. 239:14-16, July 1, 1948.

Chorionepitheliomas of the ovary may be metastatic from a uterine or ectopic pregnancy or may be a constituent tissue of an ovarian teratoma. Only 12 previous cases of primary teratomatous chorionepithelioma of the ovary have been reported. These neoplasms appear first in childhood and are manifested by precocious sexual development, onset of irregular menses, a positive Ascheim-Zondek test and the appearance of a lower abdominal mass associated with dull constant pain.

Radiation has no effect on these tumors and the only treatment to date is total hysterectomy with bilateral salpingo-oöphorectomy. The prognosis is bad without exception. 32 references. 2 figures. 1 table.—*A. N. Evans.*

THE PEDIATRIC BOOKSHELF

Lactation: Function and Product. Part I of British Medical Bulletin, Vol. 5, Number 23, 1947. London, England: William Heinemann, 10 shillings.

The British Medical Bulletin is one of the world's finest medical journals, and should receive much wider reading in this country than it does. The issue under review is divided into two parts, as they all are now. The first part consists of a scientific symposium on lactation; the second part contains miscellaneous articles, book reviews, and notes on subjects of historic bibliographic and general medical interest. The list of contributors comprises many of the leaders of British medicine, who write in a cultured essay-like style which makes for smooth easy reading.

This symposium on lactation covers the broad fields of physiology, endocrinology, biochemistry, nutrition and sanitation. There are a number of contributions from workers in the veterinary field, since much of what is known of lactational physiology in the human comes from observations on dairy cattle and other mammals. Of special interest to the pediatrician, apart from the broader physiologic discussions, are the chapters by Margaret Robinson on "Clinical treatment of hypogalactia by hormonal methods"; by Josephine Barnes on "Hormonal inhibition of lactation, with special reference to man"; by S. K. Kow, and B. S. Platt and Alan Moncrieff on "Nutritional qualities of milk"; by Harold Waller on "Incidence, causes, and prevention of failure of breast-feeding"; and by J. Smith on "Milk-borne disease in Britain". Part II contains several short articles on the history of infant feeding, by B. M. Duncan, F. N. L. Poynter, and F. Tubbs. All in all, this issue of the British Medical Bulletin represents the most up-to-date survey on the problems of human lactation to appear in recent years.

Your Child from 6 to 12. *Federal Security Agency, Social Security Administration. Children's Bureau, Washington, D. C.* Superintendent of Documents, U. S. Government Printing Office. 141 p. illus. Children's Bureau Publication #324. 20 cents. 1949.

This is an excellent guidance manual for parents. About one-fifth of its 130-odd pages are given over to physical problems, such as diet and emergency care of illness. The bulk of the text deals with behavior, discussing and giving counsel regarding everyday matters such as social adjustments, play, school, adjustments to siblings of other ages, sex attitudes, etc.

(Parents may secure single copies of this publication without charge by sending a request to U. S. Children's Bureau, Federal Security Agency, Washington, D. C. Larger number of copies must be ordered at 20 cents each from the Superintendent of Documents, U. S. Government Printing Office, Washington, D. C.—ED.)

The Biology of Melanomas. A Symposium. 466 p. illus. 1948, The New York Academy of Sciences, New York, 24, N. Y. $5.00.

All persons except the albino possess melanin pigment in the normal skin, mucous membranes, hair, eye, adrenal medulla, and leptomeninges, and also in Mongolian spots and pigmented nevi. Fortunately the pigment bearing cells only rarely give rise to malignant tumors in the childhood years —of 349 cases of malignant melanoma reported in Connecticut from 1935 to through 1946, cited in the text, only six were individuals under 15 years of age, and only three of these were under age 10; in none was the eye the primary site. This symposium reports the conference on "The Biology of Normal and Atypical Pigment Cell Growth", held by the New York Academy of Sciences in November 1946, and brings together a large mass of anatomic, evolutionary and clinical information on the pigment problem.

The Spleen and Hypersplenism. *William Dameshek and Solomon Estren, J. H. Pratt Diagnostic Hospital, Tufts College Medical School, Boston, Mass.* New York, Grune and Stratton. 55 plates printed on one side only with a plastic binder. $4.75.

Hypersplenism—"exaggerated (hormonal?) splenic functions with 'selective' or 'total' reductions of red cells, leukocytes and platelets (cytopenias)" —is now accepted as a prime mechanism in the pathogenesis of many different blood disorders. This thesis is here lucidly portrayed in a novel pictorial monograph, different from what is usual in medical publishing in that each page is a reproduction of charts, photographs, and photomicrographs as exhibited at the A.M.A. 1947 Convention and the New York Academy of Medicine October 1947. There are 55 poster-like large plates, printed on one side only, with a plastic binder.

The Challenge of Parenthood. *Rudolph Dreikurs, Professor of Psychiatry, Chicago Medical School, Chicago.* New York, Duell, Sloan & Pearce, Inc. 1948. 334 pp. $3.50.

This is a book for parents, written by a psychiatrist of the Adlerian School. The first section "The Psychological Background" discusses the psychologic mechanisms operative in the development or present-day American parents and children, and emphasizes how essential is the parents' attitude in the guidance of the child.

The second section, "The Methods of Training", is divided into three chapters, the first of which expounds certain methods of maintaining order, avoiding conflict and encouraging the child. The next chapter discusses

common mistakes made by parents, and the author's corrections. The third chapter is devoted to specific training situations which arise at the various stages in the development of all children.

The personality structures of difficult children are analyzed in the concluding section. Several case illustrations are given to describe the various types of behavior problems and the ways in which they should be treated.

The advices given are detailed and sensible, yet one wonders whether this book will help many parents whose children have behavior problems. The author pre-supposes that many parents can coldly and accurately analyze their mistakes and correct them. Indeed, the attempt to explain the problems of child-raising often does not penetrate beyond an unconvincing intellectual level.

Handbook of Child Guidance. *Ernest Harms, Editor.* Child Care Publications, New York, N. Y. 1948.

This book describes in a broad sense the theory and practice of child guidance for the normal as well as for the subnormal child. Beginning with a brief history of the development of child guidance in the United States, discussion proceeds in terms of guidance of the normal child from the nursery school age through the secondary schools with the description of the guidance of the superior child. Consideration is given of what to do for the physically handicapped as well as the so-called subnormal individual. The authors of the various chapters are workers in the fields of psychiatry, education, social work, psychology, sociology, the law and religion. The book ends with excellent reviews of the psychoanalytic viewpoint of Freud as well as the psychologies of Adler and Jung. The pediatrician and the general practitioner working with children will find the book informative, and useful in getting an overall picture of child guidance work.—*M. J. E. S.*

The Psychological Origin and Treatment of Enuresis (A Practical Discussion of Bed-wetting). *Stevenson Smith, Ph.D.* The Univ. of Washington. 1948. $1.75.

This book is a "fragmentary discussion" which leaves the reader adrift to pick and choose his way and it would take considerable previous orientation to the problem not to be confused. To cite one instance among many it strikes the reviewer that it would take an exceptional parent to gain any insight from the accusing tone of this book. Intellectual understanding alone is not enough to change emotional attitudes. After highlighting all the things a parent has done wrong, the following statement seems outstandingly naive: "We shall assume that possibly for a month now you have not mentioned bed-wetting and have adopted a radically changed policy toward managing your child. Be sure you have done this before starting any specific training. Be sure you notice a vast difference in the child's attitude toward you and the world in general. If you have played the game

right this change will have taken place". Would that it were that simple! The unwary reader might in the end have no other recourse but to turn to the chapter on the ingenious mechanical apparatuses devised to wake a child up while voiding. If a child were frightened out of bed-wetting by these, one is left to speculate as to which neuropathic trait would take its place.

Baby Care Course for Camp Fire Girls. *Rosemary Lippitt, Child Welfare Station, University of Iowa.* New York, N. Y. Camp Fire Girls, Inc. 1948. $0.75.

This is an educational booklet explaining the many different phases of baby care and how to present these phases to groups of girls ranging in age from 12 to 18 years.

Announcements

The Sixth International Congress of Pediatrics will be held in Zürich, Switzerland from July 22 to 26, 1950. It is proposed to hold two plenary sessions, each lasting half a day, and a series of simultaneous group sessions. Each group session will consist of lectures lasting from ten to thirty minutes, followed by open discussion in which no contribution may exceed five minutes. As part of the Congress there will be held a scientific exhibit lasting two weeks.

The President of the Congress in Professor G. Fanconi of Zürich and the Secretary-General is Dr. Hans Zellweger of Zürich (address: Kinderklinik, Zürich). Inquires with respect to attendance and participation in the program or the exhibit may be addressed to Dr. Zellweger.

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*Hollender, A. R.: Office Treatment of the Nose, Throat & Ear, Chicago, The Year Book Publishers, Inc., 1943, p. 316.

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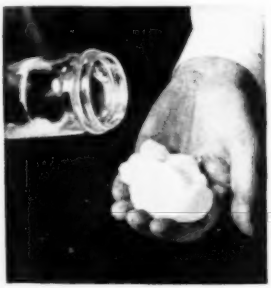

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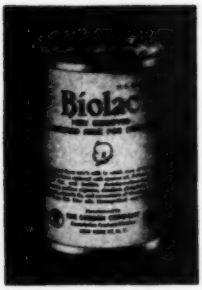

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